5756901 (171)
Access DB#

SEARCH REQUEST FORM

5690155

Scientific and Technical Information Center

12/26/01 Completed

Requester's Full Name: RITA MITRA Examiner #: 77995 Date: 12/18/01
Art Unit: 1653 Phone Number 30 605-1211 Serial Number: 09/756,185
Mail Box and Bldg/Room Location: 9B01; CM1-9B03 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEP

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Compound B as angiogenic agent in combination with human growth factors.

Inventors (please provide full names): Marina Zicheti, Silvia Donini, Francesco Borrelli

Earliest Priority Filing Date: July 9, 1998

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

patent and non-patent literature

I request a search on use of component B (an ~~agent~~) angiogenic agent in combination with human growth factor. The composition used in the treatment of wounds / ulcer / traumatic lesions.

Note: Component B was originally isolated from human urine.

Keywords:
Basic fibroblast growth factor (bFGF)
Vascular endothelial growth factor (VEGF)
Component B
wound / ulcer / angiogenesis / lesions
cicatrizant
Synergistic

POINT OF CONTACT:
BARB O'BRYEN
TECH. INFORMATION SPECIALIST
STIC CM1 ~~12C14~~ 12E18 308-4291

RECEIVED DEC 19 2001 (STIC)

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STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: BOB	NA Sequence (#)		STN	327
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up:	Bibliographic	X	Dr.Link	
Date Completed: 12-26-01	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 20	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time: 73	Other		Other (specify)	

PTO-1590 (1-2000)

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=> fil reg; d rn cn l4; d rn cn l5
FILE 'REGISTRY' ENTERED AT 15:54:51 ON 26 DEC 2001
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STRUCTURE FILE UPDATES:   25 DEC 2001  HIGHEST RN 378187-30-5
DICTIONARY FILE UPDATES:  25 DEC 2001  HIGHEST RN 378187-30-5

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   106096-93-9  REGISTRY
CN   Fibroblast growth factor, basic (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Astroglial growth factor 2
CN   Basic astroglial growth factor
CN   Basic FGF
CN   Basic fibroblast growth factor
CN   FGF 2
CN   Fibroblast growth factor 2
CN   Growth factors (animal), astroglial growth factor 2
CN   Growth factors (animal), basic fibroblast growth factor
CN   Heparin-binding growth factor 2


L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   127464-60-2  REGISTRY
CN   Vascular endothelial growth factor (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   1: PN: US6306829 SEQID: 1 claimed sequence
CN   Animal growth regulator, VEGF
CN   Animal growth regulators, glioma-derived vascular endothelial growth
     factors
CN   Animal growth regulators, VEGF
CN   Animal growth regulators, VEGF (vascular endothelial growth factor)
CN   Cytokines, vascular permeability factor
CN   Folliculo-stellate-derived growth factors
CN   FSdGF pituitary hormones
CN   Glioma-derived vascular endothelial growth factors
CN   Pituitary hormones, folliculo-stellate-derived growth factors
CN   Vascular endothelial growth factor A
CN   Vascular permeability factor
CN   Vasculotropin
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```
=> fil capl; d que l14; d que l20; d que l25; d que l26; d que l30; d que l37; d que l39
FILE 'CAPLUS' ENTERED AT 16:58:00 ON 26 DEC 2001
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FILE COVERS 1907 - 26 Dec 2001  VOL 135 ISS 26
FILE LAST UPDATED: 24 Dec 2001  (20011224/ED)
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

CAplus now provides online access to patents and literature covered in CA from 1907 to the present. Bibliographic information and abstracts were added in 2001 for over 3.8 million records from 1907-1966.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The CA Lexicon is now available in the Controlled Term (/CT) field. Enter HELP LEXICON for full details.


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L4             1 SEA FILE=REGISTRY ABB=ON  "BASIC FIBROBLAST GROWTH FACTOR"/CN
L5             1 SEA FILE=REGISTRY ABB=ON  "VASCULAR ENDOTHELIAL GROWTH
                 FACTOR"/CN
L6          7439 SEA FILE=CAPLUS ABB=ON  L4 OR (BASIC FIBROBLAST)/OBI OR
                 BFGF/OBI
L7          5886 SEA FILE=CAPLUS ABB=ON  L5 OR (VASCULAR ENDOTHELIAL GROWTH
                 FACTOR)/OBI OR VEGF
L8          4871 SEA FILE=CAPLUS ABB=ON  (COMPOUND OR COMPONENT)(W)B
L14            1 SEA FILE=CAPLUS ABB=ON  L8 AND (L6 OR L7)



L8          4871 SEA FILE=CAPLUS ABB=ON  (COMPOUND OR COMPONENT)(W)B
L18         9365 SEA FILE=CAPLUS ABB=ON  ANGIOGEN?/OBI
L20            1 SEA FILE=CAPLUS ABB=ON  L8(L)L18



L4             1 SEA FILE=REGISTRY ABB=ON  "BASIC FIBROBLAST GROWTH FACTOR"/CN
L5             1 SEA FILE=REGISTRY ABB=ON  "VASCULAR ENDOTHELIAL GROWTH
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			FACTOR"/CN
L6	7439	SEA FILE=CAPLUS ABB=ON	L4 OR (BASIC FIBROBLAST)/OBI OR BFGF/OBI
L7	5886	SEA FILE=CAPLUS ABB=ON	L5 OR (VASCULAR ENDOTHELIAL GROWTH FACTOR)/OBI OR VEGF
L11	21373	SEA FILE=CAPLUS ABB=ON	DRUG INTERACTIONS+OLD/CT
L21	161	SEA FILE=CAPLUS ABB=ON	ANGIOGENIC AGENT#
L22	50	SEA FILE=CAPLUS ABB=ON	L21 AND (L6 OR L7)
L24	78193	SEA FILE=CAPLUS ABB=ON	SYNERG?
L25	2	SEA FILE=CAPLUS ABB=ON	L22 AND (L11 OR L24)

L4	1	SEA FILE=REGISTRY ABB=ON	"BASIC FIBROBLAST GROWTH FACTOR"/CN
L5	1	SEA FILE=REGISTRY ABB=ON	"VASCULAR ENDOTHELIAL GROWTH FACTOR"/CN
L6	7439	SEA FILE=CAPLUS ABB=ON	L4 OR (BASIC FIBROBLAST)/OBI OR BFGF/OBI
L7	5886	SEA FILE=CAPLUS ABB=ON	L5 OR (VASCULAR ENDOTHELIAL GROWTH FACTOR)/OBI OR VEGF
L8	4871	SEA FILE=CAPLUS ABB=ON	(COMPOUND OR COMPONENT)(W)B
L9	5215	SEA FILE=CAPLUS ABB=ON	ANTIULCER AGENTS+OLD/CT
L10	7741	SEA FILE=CAPLUS ABB=ON	WOUND HEALING/CW
L11	21373	SEA FILE=CAPLUS ABB=ON	DRUG INTERACTIONS+OLD/CT
L12	5828	SEA FILE=CAPLUS ABB=ON	INJURY/CT OR TRAUMA/CT OR WOUND#/CT
L13	554	SEA FILE=CAPLUS ABB=ON	CICATRI?
L21	161	SEA FILE=CAPLUS ABB=ON	ANGIOGENIC AGENT#
L26	3	SEA FILE=CAPLUS ABB=ON	(L21 OR L8) AND (L6 OR L7) AND (L9 OR L10 OR L11 OR L12 OR L13)

L9	5215	SEA FILE=CAPLUS ABB=ON	ANTIULCER AGENTS+OLD/CT
L10	7741	SEA FILE=CAPLUS ABB=ON	WOUND HEALING/CW
L11	21373	SEA FILE=CAPLUS ABB=ON	DRUG INTERACTIONS+OLD/CT
L12	5828	SEA FILE=CAPLUS ABB=ON	INJURY/CT OR TRAUMA/CT OR WOUND#/CT
L13	554	SEA FILE=CAPLUS ABB=ON	CICATRI?
L15	56137	SEA FILE=CAPLUS ABB=ON	GROWTH/CW(L)(SUBSTANCE# OR REGULATOR# OR FACTOR#)
L30	4	SEA FILE=CAPLUS ABB=ON	L15(L)((L9 OR L10 OR L11 OR L12 OR L13))

L4	1	SEA FILE=REGISTRY ABB=ON	"BASIC FIBROBLAST GROWTH FACTOR"/CN
L5	1	SEA FILE=REGISTRY ABB=ON	"VASCULAR ENDOTHELIAL GROWTH FACTOR"/CN
L6	7439	SEA FILE=CAPLUS ABB=ON	L4 OR (BASIC FIBROBLAST)/OBI OR BFGF/OBI
L7	5886	SEA FILE=CAPLUS ABB=ON	L5 OR (VASCULAR ENDOTHELIAL GROWTH FACTOR)/OBI OR VEGF
L9	5215	SEA FILE=CAPLUS ABB=ON	ANTIULCER AGENTS+OLD/CT
L10	7741	SEA FILE=CAPLUS ABB=ON	WOUND HEALING/CW
L11	21373	SEA FILE=CAPLUS ABB=ON	DRUG INTERACTIONS+OLD/CT
L12	5828	SEA FILE=CAPLUS ABB=ON	INJURY/CT OR TRAUMA/CT OR WOUND#/CT
L13	554	SEA FILE=CAPLUS ABB=ON	CICATRI?
L28	5767	SEA FILE=CAPLUS ABB=ON	(L6 OR L7)(L)(BAC OR THU)/RL - Role
L33	208	SEA FILE=CAPLUS ABB=ON	(L6 OR L7)(L)(L9 OR L10 OR L11 OR L12 OR L13)
L34	116	SEA FILE=CAPLUS ABB=ON	L28 AND L33
L37	12	SEA FILE=CAPLUS ABB=ON	L6 AND L7 AND L34

BAC - biological activity

THU - Therapeutic use

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L4            1 SEA FILE=REGISTRY ABB=ON  "BASIC FIBROBLAST GROWTH FACTOR"/CN
L5            1 SEA FILE=REGISTRY ABB=ON  "VASCULAR ENDOTHELIAL GROWTH
                FACTOR"/CN
L6         7439 SEA FILE=CAPLUS ABB=ON  L4 OR (BASIC FIBROBLAST)/OBI OR
                BFGF/OBI
L7         5886 SEA FILE=CAPLUS ABB=ON  L5 OR (VASCULAR ENDOTHELIAL GROWTH
                FACTOR)/OBI OR VEGF
L9         5215 SEA FILE=CAPLUS ABB=ON  ANTIULCER AGENTS+OLD/CT
L10        7741 SEA FILE=CAPLUS ABB=ON  WOUND HEALING/CW
L11       21373 SEA FILE=CAPLUS ABB=ON  DRUG INTERACTIONS+OLD/CT
L12        5828 SEA FILE=CAPLUS ABB=ON  INJURY/CT OR TRAUMA/CT OR WOUND#/CT
L13         554 SEA FILE=CAPLUS ABB=ON  CICATRI?
L18        9365 SEA FILE=CAPLUS ABB=ON  ANGIOGEN?/OBI
L28        5767 SEA FILE=CAPLUS ABB=ON  (L6 OR L7)(L)(BAC OR THU)/RL
L33         208 SEA FILE=CAPLUS ABB=ON  (L6 OR L7)(L)(L9 OR L10 OR L11 OR L12
                OR L13)
L34         116 SEA FILE=CAPLUS ABB=ON  L28 AND L33
L38          31 SEA FILE=CAPLUS ABB=ON  L34 AND PHARMAC?/SC
L39          10 SEA FILE=CAPLUS ABB=ON  L18 AND L38


=> s l14 or l20 or l25 or l26 or l30 or l37 or l39
L137         29 L14 OR L20 OR L25 OR L26 OR L30 OR L37 OR L39

=> fil medl
FILE 'MEDLINE' ENTERED AT 16:58:19 ON 26 DEC 2001

 FILE LAST UPDATED: 24 DEC 2001 (20011224/UP).  FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records.  See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week.  A new current-awareness alert
 frequency (EVERYUPDATE) is available.  See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> d que l51; d que l52; d que l72; d que l63; d que l65; d que l69; d que l73
L40          378 SEA FILE=MEDLINE ABB=ON  (COMPOUND OR COMPONENT)(W)B
L48         5950 SEA FILE=MEDLINE ABB=ON  FIBROBLAST GROWTH FACTOR, BASIC/CT
L49         4712 SEA FILE=MEDLINE ABB=ON  ENDOTHELIAL GROWTH FACTORS/CT
L51            0 SEA FILE=MEDLINE ABB=ON  L40 AND (L48 OR L49)



L40          378 SEA FILE=MEDLINE ABB=ON  (COMPOUND OR COMPONENT)(W)B
L41         1712 SEA FILE=MEDLINE ABB=ON  (COMPOUND OR COMPONENT)(W)A
L42          206 SEA FILE=MEDLINE ABB=ON  L40 NOT L41
L43        35916 SEA FILE=MEDLINE ABB=ON  WOUND HEALING/CT
L44        10173 SEA FILE=MEDLINE ABB=ON  CICATRIX+NT/CT
L45       387996 SEA FILE=MEDLINE ABB=ON  "WOUNDS AND INJURIES"+NT/CT
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L46	5465	SEA FILE=MEDLINE ABB=ON	ULCER/CT
L47	17224	SEA FILE=MEDLINE ABB=ON	SKIN ULCER+NT/CT
L52	0	SEA FILE=MEDLINE ABB=ON	L42 AND (L43 OR L44 OR L45 OR L46 OR L47)

L40	378	SEA FILE=MEDLINE ABB=ON	(COMPOUND OR COMPONENT)(W)B
L70	2649	SEA FILE=MEDLINE ABB=ON	NEOVASCULARIZATION, PHYSIOLOGIC/CT
L72	0	SEA FILE=MEDLINE ABB=ON	L40 AND L70

L43	35916	SEA FILE=MEDLINE ABB=ON	WOUND HEALING/CT
L44	10173	SEA FILE=MEDLINE ABB=ON	CICATRIX+NT/CT
L45	387996	SEA FILE=MEDLINE ABB=ON	"WOUNDS AND INJURIES"+NT/CT
L46	5465	SEA FILE=MEDLINE ABB=ON	ULCER/CT
L47	17224	SEA FILE=MEDLINE ABB=ON	SKIN ULCER+NT/CT
L49	4712	SEA FILE=MEDLINE ABB=ON	ENDOTHELIAL GROWTH FACTORS/CT
L56	937	SEA FILE=MEDLINE ABB=ON	L49(L)(AD OR TU OR PD)/CT
L59	15040	SEA FILE=MEDLINE ABB=ON	((L43 OR L44 OR L45 OR L46 OR L47))(L)DT/CT
L63	3	SEA FILE=MEDLINE ABB=ON	L56 AND L59

Subheadings
AD - administration & dosage
TU - therapeutic use
PD - pharmacology
DE = drug effects

L43	35916	SEA FILE=MEDLINE ABB=ON	WOUND HEALING/CT
L49	4712	SEA FILE=MEDLINE ABB=ON	ENDOTHELIAL GROWTH FACTORS/CT
L56	937	SEA FILE=MEDLINE ABB=ON	L49(L)(AD OR TU OR PD)/CT
L64	5621	SEA FILE=MEDLINE ABB=ON	L43(L)DE/CT
L65	9	SEA FILE=MEDLINE ABB=ON	L56 AND L64

L43	35916	SEA FILE=MEDLINE ABB=ON	WOUND HEALING/CT
L44	10173	SEA FILE=MEDLINE ABB=ON	CICATRIX+NT/CT
L45	387996	SEA FILE=MEDLINE ABB=ON	"WOUNDS AND INJURIES"+NT/CT
L46	5465	SEA FILE=MEDLINE ABB=ON	ULCER/CT
L47	17224	SEA FILE=MEDLINE ABB=ON	SKIN ULCER+NT/CT
L48	5950	SEA FILE=MEDLINE ABB=ON	FIBROBLAST GROWTH FACTOR, BASIC/CT
L55	3068	SEA FILE=MEDLINE ABB=ON	L48(L)(AD OR TU OR PD)/CT
L57	1457	SEA FILE=MEDLINE ABB=ON	L55/MAJ
L59	15040	SEA FILE=MEDLINE ABB=ON	((L43 OR L44 OR L45 OR L46 OR L47))(L)DT/CT
L60	8430	SEA FILE=MEDLINE ABB=ON	L59/MAJ
L61	25	SEA FILE=MEDLINE ABB=ON	L57 AND L60
L64	5621	SEA FILE=MEDLINE ABB=ON	L43(L)DE/CT
L66	2836	SEA FILE=MEDLINE ABB=ON	L64/MAJ
L67	40	SEA FILE=MEDLINE ABB=ON	L57 AND L66
L69	4	SEA FILE=MEDLINE ABB=ON	L61 AND L67

L43	35916	SEA FILE=MEDLINE ABB=ON	WOUND HEALING/CT
L44	10173	SEA FILE=MEDLINE ABB=ON	CICATRIX+NT/CT
L45	387996	SEA FILE=MEDLINE ABB=ON	"WOUNDS AND INJURIES"+NT/CT
L46	5465	SEA FILE=MEDLINE ABB=ON	ULCER/CT
L47	17224	SEA FILE=MEDLINE ABB=ON	SKIN ULCER+NT/CT
L48	5950	SEA FILE=MEDLINE ABB=ON	FIBROBLAST GROWTH FACTOR, BASIC/CT
L55	3068	SEA FILE=MEDLINE ABB=ON	L48(L)(AD OR TU OR PD)/CT
L57	1457	SEA FILE=MEDLINE ABB=ON	L55/MAJ
L59	15040	SEA FILE=MEDLINE ABB=ON	((L43 OR L44 OR L45 OR L46 OR L47))(L)DT/CT

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L60        8430 SEA FILE=MEDLINE ABB=ON  L59/MAJ
L61          25 SEA FILE=MEDLINE ABB=ON  L57 AND L60
L64        5621 SEA FILE=MEDLINE ABB=ON  L43(L)DE/CT
L66        2836 SEA FILE=MEDLINE ABB=ON  L64/MAJ
L67          40 SEA FILE=MEDLINE ABB=ON  L57 AND L66
L68          61 SEA FILE=MEDLINE ABB=ON  L61 OR L67
L70        2649 SEA FILE=MEDLINE ABB=ON  NEOVASCULARIZATION, PHYSIOLOGIC/CT
L73           5 SEA FILE=MEDLINE ABB=ON  L68 AND L70


=> s l63 or l65 or l69 or l73
L138         18 L63 OR L65 OR L69 OR L73

=> fil wpids; d que l84; d que l87; d que l89;d que l94; s l84 or l87 or l89 or l94
FILE 'WPIDS' ENTERED AT 16:59:04 ON 26 DEC 2001
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FILE LAST UPDATED: 20 DEC 2001              <20011220/UP>
MOST RECENT DERWENT UPDATE          200175   <200175/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SDI'S MAY BE RUN ON EVERY UPDATE OR MONTHLY AS OF JUNE 2001.
    (EVERY UPDATE IS THE DEFAULT). FOR PRICING INFORMATION
    SEE HELP COST <<<

>>> FOR UP-TO-DATE INFORMATION ABOUT THE DERWENT CHEMISTRY
    RESOURCE, PLEASE VISIT
         http://www.derwent.com/chemistryresource/index.html <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<


L74       21406 SEA FILE=WPIDS ABB=ON  (COMPOUND OR COMPONENT)(W)B
L75        2456 SEA FILE=WPIDS ABB=ON  (COMPOUND OR COMPONENT)(W)A
L76       19861 SEA FILE=WPIDS ABB=ON  L74 NOT L75
L81         441 SEA FILE=WPIDS ABB=ON  BASIC FIBROBLAST OR BFGF
L82         648 SEA FILE=WPIDS ABB=ON  VASCULAR ENDOTHELIAL GROWTH FACTOR OR
                VEGF
L84           4 SEA FILE=WPIDS ABB=ON  L76 AND (L81 OR L82)



L74       21406 SEA FILE=WPIDS ABB=ON  (COMPOUND OR COMPONENT)(W)B
L75        2456 SEA FILE=WPIDS ABB=ON  (COMPOUND OR COMPONENT)(W)A
L76       19861 SEA FILE=WPIDS ABB=ON  L74 NOT L75
L77      117914 SEA FILE=WPIDS ABB=ON  WOUND OR WOUNDS
L78        2912 SEA FILE=WPIDS ABB=ON  ANGIOGEN?
L79         681 SEA FILE=WPIDS ABB=ON  CICATRI?
L80       13324 SEA FILE=WPIDS ABB=ON  ULCER?
L86          13 SEA FILE=WPIDS ABB=ON  L76 AND L78
L87           4 SEA FILE=WPIDS ABB=ON  L86 AND (L77 OR L79 OR L80)



L74       21406 SEA FILE=WPIDS ABB=ON  (COMPOUND OR COMPONENT)(W)B
L75        2456 SEA FILE=WPIDS ABB=ON  (COMPOUND OR COMPONENT)(W)A
L76       19861 SEA FILE=WPIDS ABB=ON  L74 NOT L75
L77      117914 SEA FILE=WPIDS ABB=ON  WOUND OR WOUNDS
L79         681 SEA FILE=WPIDS ABB=ON  CICATRI?
L80       13324 SEA FILE=WPIDS ABB=ON  ULCER?
L88       11646 SEA FILE=WPIDS ABB=ON  GROWTH(W)(FACTOR# OR SUBSTANCE# OR
                REGULATOR#)
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L89          7 SEA FILE=WPIDS ABB=ON  L76 AND L88 AND (L77 OR L79 OR L80)


L74      21406 SEA FILE=WPIDS ABB=ON  (COMPOUND OR COMPONENT)(W)B
L77     117914 SEA FILE=WPIDS ABB=ON  WOUND OR WOUNDS
L78       2912 SEA FILE=WPIDS ABB=ON  ANGIOGEN?
L79        681 SEA FILE=WPIDS ABB=ON  CICATRI?
L80      13324 SEA FILE=WPIDS ABB=ON  ULCER?
L90      14029 SEA FILE=WPIDS ABB=ON  URINE
L91         33 SEA FILE=WPIDS ABB=ON  L74 AND L90
L92          3 SEA FILE=WPIDS ABB=ON  L91 AND (L77 OR L78 OR L79 OR L80)
L93      14167 SEA FILE=WPIDS ABB=ON  FUNGI
L94          2 SEA FILE=WPIDS ABB=ON  L92 NOT L93


L139        11 L84 OR L87 OR L89 OR L94

=> fil embase; d que l104; d que l106; d que l133; d que l111; d que l119; d que l134; d
que l136; s l104 or l133 or l111 or l119 or l134 or l136
FILE 'EMBASE' ENTERED AT 16:59:41 ON 26 DEC 2001
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 FILE COVERS 1974 TO 20 Dec 2001 (20011220/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L95          356 SEA FILE=EMBASE ABB=ON  (COMPOUND OR COMPONENT)(W)B
L101        6002 SEA FILE=EMBASE ABB=ON  BASIC FIBROBLAST GROWTH FACTOR/CT
L102        5478 SEA FILE=EMBASE ABB=ON  VASCULOTROPIN/CT
L104           1 SEA FILE=EMBASE ABB=ON  L95 AND (L101 OR L102)


L95          356 SEA FILE=EMBASE ABB=ON  (COMPOUND OR COMPONENT)(W)B
L96         1693 SEA FILE=EMBASE ABB=ON  (COMPOUND OR COMPONENT)(W)A
L103       11434 SEA FILE=EMBASE ABB=ON  ANGIOGENESIS/CT
L105         208 SEA FILE=EMBASE ABB=ON  L95 NOT L96
L106           0 SEA FILE=EMBASE ABB=ON  L105 AND L103


L95          356 SEA FILE=EMBASE ABB=ON  (COMPOUND OR COMPONENT)(W)B
L96         1693 SEA FILE=EMBASE ABB=ON  (COMPOUND OR COMPONENT)(W)A
L97        21682 SEA FILE=EMBASE ABB=ON  WOUND HEALING+NT/CT
L98        61073 SEA FILE=EMBASE ABB=ON  ULCER+NT/CT
L99         2425 SEA FILE=EMBASE ABB=ON  DECUBITUS/CT
L100      418542 SEA FILE=EMBASE ABB=ON  INJURY+NT/CT
L105         208 SEA FILE=EMBASE ABB=ON  L95 NOT L96
L130        2337 SEA FILE=EMBASE ABB=ON  ULCER HEALING/CT
L133           6 SEA FILE=EMBASE ABB=ON  ((L97 OR L98 OR L99 OR L100) OR L130)
                 AND L105


L95          356 SEA FILE=EMBASE ABB=ON  (COMPOUND OR COMPONENT)(W)B
L108      139680 SEA FILE=EMBASE ABB=ON  URINE
L109           7 SEA FILE=EMBASE ABB=ON  L95 AND L108
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L110          3 SEA FILE=EMBASE ABB=ON  THORMAHLEN/CT
L111          1 SEA FILE=EMBASE ABB=ON  L109 AND L110


L101       6002 SEA FILE=EMBASE ABB=ON  BASIC FIBROBLAST GROWTH FACTOR/CT
L102       5478 SEA FILE=EMBASE ABB=ON  VASCULOTROPIN/CT
L103      11434 SEA FILE=EMBASE ABB=ON  ANGIOGENESIS/CT
L113       3336 SEA FILE=EMBASE ABB=ON  URINE(3A)PROTEIN#
L118          7 SEA FILE=EMBASE ABB=ON  L103 AND L113
L119          3 SEA FILE=EMBASE ABB=ON  (L102 OR L101) AND L118


L97       21682 SEA FILE=EMBASE ABB=ON  WOUND HEALING+NT/CT
L98       61073 SEA FILE=EMBASE ABB=ON  ULCER+NT/CT
L99        2425 SEA FILE=EMBASE ABB=ON  DECUBITUS/CT
L100     418542 SEA FILE=EMBASE ABB=ON  INJURY+NT/CT
L101       6002 SEA FILE=EMBASE ABB=ON  BASIC FIBROBLAST GROWTH FACTOR/CT
L102       5478 SEA FILE=EMBASE ABB=ON  VASCULOTROPIN/CT
L121        193 SEA FILE=EMBASE ABB=ON  L101(L)DT/CT
L122        133 SEA FILE=EMBASE ABB=ON  L102(L)DT/CT
L130       2337 SEA FILE=EMBASE ABB=ON  ULCER HEALING/CT
L134          3 SEA FILE=EMBASE ABB=ON  ((L97 OR L98 OR L99 OR L100) OR L130)
                AND L121 AND L122


L97       21682 SEA FILE=EMBASE ABB=ON  WOUND HEALING+NT/CT
L98       61073 SEA FILE=EMBASE ABB=ON  ULCER+NT/CT
L99        2425 SEA FILE=EMBASE ABB=ON  DECUBITUS/CT
L100     418542 SEA FILE=EMBASE ABB=ON  INJURY+NT/CT
L101       6002 SEA FILE=EMBASE ABB=ON  BASIC FIBROBLAST GROWTH FACTOR/CT
L102       5478 SEA FILE=EMBASE ABB=ON  VASCULOTROPIN/CT
L103      11434 SEA FILE=EMBASE ABB=ON  ANGIOGENESIS/CT
L121        193 SEA FILE=EMBASE ABB=ON  L101(L)DT/CT
L122        133 SEA FILE=EMBASE ABB=ON  L102(L)DT/CT
L125     344450 SEA FILE=EMBASE ABB=ON  L97/MAJ OR L98/MAJ OR L99/MAJ OR
                L100/MAJ
L130       2337 SEA FILE=EMBASE ABB=ON  ULCER HEALING/CT
L135     344539 SEA FILE=EMBASE ABB=ON  L130/MAJ OR L125
L136         16 SEA FILE=EMBASE ABB=ON  L135 AND (L121 OR L122) AND L103


L140         30 L104 OR L133 OR L111 OR L119 OR L134 OR L136

=> dup rem l138,l137,l140,l139
FILE 'MEDLINE' ENTERED AT 16:59:58 ON 26 DEC 2001

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PROCESSING COMPLETED FOR L138
PROCESSING COMPLETED FOR L137
PROCESSING COMPLETED FOR L140
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Subheading DT - drug therapy

PROCESSING COMPLETED FOR L139
L141 83 DUP REM L138 L137 L140 L139 (5 DUPLICATES REMOVED)
ANSWERS '1-18' FROM FILE MEDLINE
ANSWERS '19-45' FROM FILE CAPLUS
ANSWERS '46-73' FROM FILE EMBASE
ANSWERS '74-83' FROM FILE WPIDS

=> d ibib ab hitrn 1-83; fil hom

L141 ANSWER 1 OF 83 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999148331 MEDLINE
DOCUMENT NUMBER: 99148331 PubMed ID: 10025464
TITLE: Vascular endothelial growth factor is more important than basic fibroblastic growth factor during ischemic wound healing.
AUTHOR: Corral C J; Siddiqui A; Wu L; Farrell C L; Lyons D; Mustoe T A
CORPORATE SOURCE: Division of Plastic Surgery and Reconstructive Surgery, Northwestern University Medical School, Chicago, Ill, USA.
CONTRACT NUMBER: GM-41303 (NIGMS)
SOURCE: ARCHIVES OF SURGERY, (1999 Feb) 134 (2) 200-5.
Journal code: 8IA; 9716528. ISSN: 0004-0010.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990318

AB OBJECTIVES: To test the influence of vascular endothelial growth factor (VEGF) on normal and ischemic wounds in a noncontractive dermal ulcer standardized model in the rabbit ear and to assay the levels of both VEGF and basic fibroblastic growth factor messenger RNA levels in normal and ischemic wounds at different intervals during the healing process. DESIGN AND INTERVENTIONS: Dermal ulcers were created in the normal and ischemic ears of 20 anesthetized young female New Zealand white rabbits. Either VEGF 121, VEGF 165 (30 microg per wound), or buffered saline solution alone was applied to each wound and covered. Wounds were harvested at day 7 or 10 and evaluated histologically. Twenty-four similar rabbits were wounded in the same manner and their untreated wounds were harvested at 1, 3, 7, and 10 days after wounding. The wounds were analyzed with reverse transcriptase polymerase chain reaction. MAIN OUTCOME MEASURES: Histologic specimens were measured for amount of new epithelium and granulation tissue. Reverse transcriptase polymerase chain reaction was used to determine basic fibroblastic growth factor and VEGF messenger RNA expression. RESULTS: Both isoforms of VEGF improved granulation tissue formation in both normal and ischemic wounds with a magnitude similar to other vulnerary agents tested in the past. Vascular endothelial growth factor application had no effect on new epithelium formation. In contrast to basic fibroblastic growth factor, VEGF messenger RNA levels were induced 4 fold by ischemia alone and 6 fold by wounding in both ischemic and normal wounds. CONCLUSION: Vascular endothelial growth factor seems to be more important than basic fibroblastic growth factor during ischemic wound healing. Treatment of ischemic wounds with VEGF improves the deficit in wound healing produced by ischemia.

L141 ANSWER 2 OF 83 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 96396453 MEDLINE
DOCUMENT NUMBER: 96396453 PubMed ID: 8803573
TITLE: Influence of vascular endothelial growth factor on bovine corneal endothelial cells in a wound-healing model.
AUTHOR: Bednarz J; Thalmann-Goetsch A; Richard G; Engelmann K

CORPORATE SOURCE: Universitats-Augenklinik Hamburg, Germany.
SOURCE: GERMAN JOURNAL OF OPHTHALMOLOGY, (1996 May) 5 (3) 127-31.
Journal code: BNO; 9206441. ISSN: 0941-2921.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961121

AB In this study we determined the influence of vascular endothelial growth factor (VEGF) on bovine corneal endothelial cell proliferation and wound healing. Proliferation was determined by measurement of DNA replication as well as by counting of the number of cells present after a defined growth period. In a wound-healing model, reproducible cell-free areas were created within monolayers of cultured bovine corneal endothelial cells and the migration of the cells into these areas was analyzed. The DNA replication and cell proliferation of bovine corneal endothelial cells were not influenced by VEGF. In contrast, in the wound-healing model, VEGF supplementation at concentrations of 1 and 10 ng/ml increased the cell density of the wounded area by 20% and 50%, respectively, as compared with the cell density of wounds left untreated by VEGF. Furthermore, no increase in DNA replication was found in cells involved in wound healing. Our results demonstrate that healing of bovine corneal endothelial cell layers after wounding is predominantly performed by cell migration rather than by proliferation. This migration can be stimulated by the addition of exogenous VEGF.

L141 ANSWER 3 OF 83 MEDLINE
ACCESSION NUMBER: 2001433596 MEDLINE
DOCUMENT NUMBER: 21373915 PubMed ID: 11481234
TITLE: Suppression of angiogenesis, tumor growth, and wound healing by resveratrol, a natural compound in red wine and grapes.
AUTHOR: Brakenhielm E; Cao R; Cao Y
CORPORATE SOURCE: Laboratory of Angiogenesis Research, Microbiology and Tumor Biology Center, Karolinska Institute, S-171 77 Stockholm, Sweden.
SOURCE: FASEB JOURNAL, (2001 Aug) 15 (10) 1798-800.
Journal code: FAS; 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20010903
Entered Medline: 20010830

L141 ANSWER 4 OF 83 MEDLINE
ACCESSION NUMBER: 2001498258 MEDLINE
DOCUMENT NUMBER: 21431854 PubMed ID: 11547309
TITLE: Healing of a free tracheal autograft is enhanced by topical vascular endothelial growth factor in an experimental rabbit model.
AUTHOR: Dodge-Khatami A; Backer C L; Holinger L D; Mavroudis C; Cook K E; Crawford S E
CORPORATE SOURCE: Northwestern University Medical School, Department of Surgery, Division of Cardiovascular-Thoracic Surgery, Children's Memorial Hospital, Chicago, Ill 60614-3394, USA.
SOURCE: JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, (2001 Sep) 122 (3) 554-61.

Journal code: K9J; 0376343. ISSN: 0022-5223.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010910
Last Updated on STN: 20011015
Entered Medline: 20011011

AB OBJECTIVE: In 1996, we introduced the free tracheal autograft technique for repair of congenital tracheal stenosis from complete tracheal rings in infants and children. Sources of possible concern with this procedure include the potential for autograft ischemia, patch dehiscence, and recurrent stenosis. Vascular endothelial growth factor is a potent angiogenic inducer (particularly in the setting of ischemia, hypoxia, or both) and is postulated to promote tissue healing. The purpose of this study was to test the hypothesis that pretreatment of tracheal autografts with topical vascular endothelial growth factor would enhance tracheal healing. METHODS: In a rabbit model of tracheal reconstruction (n = 32), an elliptically shaped portion of the anterior tracheal wall was excised. The excised portion of trachea was one third of the tracheal circumference and 2 cm in length (6 tracheal rings). This portion of trachea (the autograft) was soaked in either vascular endothelial growth factor (5 microg/mL, n = 16) or normal saline solution (n = 16) for 15 minutes before being reimplanted in the resultant tracheal opening. Animals were killed and autografts were examined at 2 weeks, 1 month, and 2 months postoperatively for gross and microscopic characteristics. RESULTS: By 2 weeks, and progressing through 1 and 2 months, autografts treated with vascular endothelial growth factor, as compared with control autografts, had reduced luminal stenosis, submucosal fibrosis, and inflammatory infiltrate (P <.05). The autografts tended to become malaligned in control animals, whereas the tracheal architecture was preserved in rabbits treated with vascular endothelial growth factor. Microvascular vessel density was significantly greater in all vascular endothelial growth factor groups (P <.05) at all time intervals. CONCLUSIONS: Topical treatment of free tracheal autografts with vascular endothelial growth factor in a rabbit tracheal reconstruction model enhanced healing, as evidenced by accelerated autograft revascularization, reduced submucosal fibrosis and inflammation, and preservation of the normal tracheal architecture. Topical vascular endothelial growth factor may improve future results of tracheal reconstruction.

L141 ANSWER 5 OF 83 MEDLINE
ACCESSION NUMBER: 2001521881 MEDLINE
DOCUMENT NUMBER: 21452924 PubMed ID: 11568077
TITLE: Gelatin sheet incorporating basic fibroblast growth factor enhances healing of devascularized sternum in diabetic rats.
AUTHOR: Iwakura A; Tabata Y; Tamura N; Doi K; Nishimura K; Nakamura T; Shimizu Y; Fujita M; Komeda M
CORPORATE SOURCE: Department of Cardiovascular Surgery, Kyoto University Graduate School of Medicine, Kyoto, Japan.
SOURCE: CIRCULATION, (2001 Sep 18) 104 (12 Suppl 1) I325-9.
Journal code: DAW; 0147763. ISSN: 1524-4539.
PUB. COUNTRY: United States
(EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010925
Last Updated on STN: 20011008
Entered Medline: 20011004

AB BACKGROUND: Poor healing of the sternum often limits the use of bilateral internal thoracic arteries (BITAs) after coronary bypass surgery in diabetic patients. We have reported that a gelatin sheet that incorporates basic fibroblast growth factor (bFGF) accelerates sternal healing after BITA removal in normal rats. This study evaluated the effects of the above method for sternal healing in diabetic animals. METHODS AND RESULTS: Diabetic Wistar rats with blood glucose levels >400 mg/dL and body-weight loss >20 g were established by a single intravenous injection of streptozotocin (55 mg/kg). After median sternotomy and BITA removal, 16 diabetic rats received either a gelatin sheet that incorporated bFGF (100 &mgr;g/sheet) on the posterior table of the sternum (FGF group, n=9) or no gelatin sheet (control, n=7). Peristernal blood flow, as measured by a noncontact laser Doppler 4 weeks after surgery in the FGF group, recovered to the preoperative level (106+/-10% versus 82+/-9%, P<0.01), and marked angiogenesis was also observed around the sternum in the FGF group (30.5+/-3.2 versus 15.8+/-2.7 vessels/unit area, P<0.01). Deep sternal wound complications developed in 5 control rats but only in 1 rat in the FGF group (P<0.05). In the FGF group, histological examination showed improved sternal healing (excellent in 6 rats and slow/poor healing in 3). Bone mineral content as assessed by dual-energy x-ray absorptometry was greater in the FGF group (75.9+/-18.1 versus 48.9+/-10.7 mg, P<0.05). Bone mineral density of the sternum was similar between the 2 groups. CONCLUSIONS: A gelatin sheet that incorporates bFGF may offset sternal ischemia and accelerate sternal bone regeneration and healing, even in diabetic patients.

L141 ANSWER 6 OF 83 MEDLINE
ACCESSION NUMBER: 2000246354 MEDLINE
DOCUMENT NUMBER: 20246354 PubMed ID: 10786682
TITLE: PTK787/ZK 222584, a novel and potent inhibitor of vascular endothelial growth factor receptor tyrosine kinases, impairs vascular endothelial growth factor-induced responses and tumor growth after oral administration.
AUTHOR: Wood J M; Bold G; Buchdunger E; Cozens R; Ferrari S; Frei J; Hofmann F; Mestan J; Mett H; O'Reilly T; Persohn E; Rosel J; Schnell C; Stover D; Theuer A; Towbin H; Wenger F; Woods-Cook K; Menrad A; Siemeister G; Schirner M; Thierauch K H; Schneider M R; Drevs J; Martiny-Baron G; Totzke F
CORPORATE SOURCE: Oncology Research, Novartis Pharma AG, Basel, Switzerland.
SOURCE: CANCER RESEARCH, (2000 Apr 15) 60 (8) 2178-89.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000511

AB PTK787/ZK 222584 (1-[4-chloroanilino]-4-[4-pyridylmethyl] phthalazine succinate) is a potent inhibitor of vascular endothelial growth factor (VEGF) receptor tyrosine kinases, active in the submicromolar range. It also inhibits other class III kinases, such as the platelet-derived growth factor (PDGF) receptor beta tyrosine kinase, c-Kit, and c-Fms, but at higher concentrations. It is not active against kinases from other receptor families, such as epidermal growth factor receptor, fibroblast growth factor receptor-1, c-Met, and Tie-2, or intracellular kinases such as c-Src, c-Abl, and protein kinase C-alpha. PTK787/ZK 222584 inhibits VEGF-induced autophosphorylation of kinase insert domain-containing receptor (KDR), endothelial cell proliferation, migration, and survival in the nanomolar range in cell-based assays. In concentrations up to 1 microM, PTK787/ZK 222584 does not have any cytotoxic or antiproliferative effect on cells that do not express VEGF receptors. After oral dosing (50

mg/kg) to mice, plasma concentrations of PTK787/ZK 222584 remain above 1 microM for more than 8 h. PTK787/ZK 222584 induces dose-dependent inhibition of VEGF and PDGF-induced angiogenesis in a growth factor implant model, as well as a tumor cell-driven angiogenesis model after once-daily oral dosing (25-100 mg/kg). In the same dose range, it also inhibits the growth of several human carcinomas, grown s.c. in nude mice, as well as a murine renal carcinoma and its metastases in a syngeneic, orthotopic model. Histological examination of tumors revealed inhibition of microvessel formation in the interior of the tumor. PTK787/ZK 222584 is very well tolerated and does not impair wound healing. It also does not have any significant effects on circulating blood cells or bone marrow leukocytes as a single agent or impair hematopoetic recovery after concomitant cytotoxic anti-cancer agent challenge. This novel compound has therapeutic potential for the treatment of solid tumors and other diseases where angiogenesis plays an important role.

L141 ANSWER 7 OF 83 MEDLINE
ACCESSION NUMBER: 2000463487 MEDLINE
DOCUMENT NUMBER: 20468532 PubMed ID: 11016317
TITLE: Basic fibroblast growth factor may improve devascularized sternal healing.
AUTHOR: Iwakura A; Tabata Y; Nishimura K; Nakamura T; Shimizu Y; Fujita M; Komeda M
CORPORATE SOURCE: Department of Cardiovascular Surgery, Kyoto University Graduate School of Medicine and Institute for Frontier Medical Sciences and College of Medical Technology, Kyoto University, Japan.
SOURCE: ANNALS OF THORACIC SURGERY, (2000 Sep) 70 (3) 824-8. Journal code: 683; 15030100R. ISSN: 0003-4975.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001017

AB BACKGROUND: We have shown that a gelatin sheet incorporating basic fibroblast growth factor enhanced bone regeneration of the devascularized sternum. The purpose of this study was to determine if topical use of the gelatin sheet accelerated normal sternal regeneration and bone remodeling. METHODS: Thirty Wistar rats had median sternotomy and were divided into 3 groups: 10 had the bilateral internal thoracic arteries removed and basic fibroblast growth factor sheet applied on the sternum (group A), 10 had just the bilateral internal thoracic arteries removed (group B), and 10 had intact bilateral internal thoracic arteries (group C). RESULTS: Four weeks later the peristernal blood flow significantly increased and marked angiogenesis was seen around the sternum in group A. Histologically, the sternum was almost completely healed only in group A. In group A the bone mineral content was highest, but the bone mineral density was similar to that in other groups. The osteoclast index in group A was highest at the border zone of bone formation and remained high in regenerated bone. CONCLUSIONS: The basic fibroblast growth factor sheet offset sternal ischemia and accelerated normal sternal bone regeneration and remodeling, not only by callus formation but also by callus resorption.

L141 ANSWER 8 OF 83 MEDLINE
ACCESSION NUMBER: 2001059791 MEDLINE
DOCUMENT NUMBER: 20536804 PubMed ID: 11082406
TITLE: Novel method to enhance sternal healing after harvesting bilateral internal thoracic arteries with use of basic fibroblast growth factor.
AUTHOR: Iwakura A; Tabata Y; Miyao M; Ozeki M; Tamura N; Ikai A;

Nishimura K; Nakamura T; Shimizu Y; Fujita M; Komeda M
CORPORATE SOURCE: Department of Cardiovascular Surgery, Kyoto University Graduate School of Medicine, Kyoto, Japan.
SOURCE: CIRCULATION, (2000 Nov 7) 102 (19 Suppl 3) III307-11.
Journal code: DAW; 0147763. ISSN: 1524-4539.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010521
Entered Medline: 20001228

AB BACKGROUND: Poor healing of the sternum often limits the use of bilateral internal thoracic arteries (BITAs) in coronary bypass surgery, especially for diabetic patients. We have reported that basic fibroblast growth factor (bFGF) enhanced regeneration of the skull. This study was designed to evaluate the effects of topical use of bFGF on sternal healing after removing the BITAs. METHODS AND RESULTS: Forty-five Wistar rats were subjected to median sternotomy and were divided into 3 groups: 15 had the BITAs removed and had a bFGF sheet applied on the posterior table of the sternum (group A), 15 had just the BITAs removed (group B), and 15 had intact BITAs (group C). Five and 10 rats were euthanized 2 and 4 weeks after surgery, respectively, in all 3 groups. Peristernal blood flow, measured with use of a noncontact laser flowmeter, decreased after removal of the BITAs (P:<0.001). Four weeks after the surgery, PBF markedly increased only in group A (9.7+/-1.2, 6.5+/-0.6, and 8.2+/-0.5 mL x min(-1) x 100 g(-1) for groups A, B, and C, respectively; P:<0.01 by ANOVA). Four weeks after surgery, the following findings were obtained only in group A: (1) nearly completely healed sternum filled with regenerated bone tissue, (2) marked angiogenesis around the sternum, and (3) osteoblasts in an active form around the edge of the sternum. CONCLUSIONS: The results suggest that use of the bFGF sheet offset the sternal ischemia and accelerated sternal healing. This method may help to decrease sternal necrosis in high-risk patients or allow extended use of BITAs in coronary bypass surgery.

L141 ANSWER 9 OF 83 MEDLINE
ACCESSION NUMBER: 2000126560 MEDLINE
DOCUMENT NUMBER: 20126560 PubMed ID: 10660723
TITLE: Use of growth factors to improve muscle healing after strain injury.
AUTHOR: Kasemkijwattana C; Menetrey J; Bosch P; Somogyi G; Moreland M S; Fu F H; Buranapanitkit B; Watkins S S; Huard J
CORPORATE SOURCE: Department of Orthopaedic Surgery, University of Pittsburgh, PA 15261, USA.
CONTRACT NUMBER: 1P60 AR44811-01 (NIAMS)
SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (2000 Jan) (370) 272-85.
Journal code: DFY; 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000216

AB Muscle injuries represent a large number of professional and recreational sports injuries. Muscle strains habitually occur after an eccentric contraction, which often leads to an injury located in the myotendinous junction. Treatment varies widely, depending on the severity of the trauma, but has remained limited mostly to rest, ice, compression,

elevation, antiinflammatory drugs, and mobilization. The authors' research group aims to develop new biologic approaches to improve muscle healing after injuries, including muscle strains. To achieve this goal, the authors investigated several parameters that will lead to the development of new strategies to enhance muscle healing. The authors first evaluated natural muscle healing after strain injuries and showed that muscle regeneration occurs in the early phase of healing but becomes impaired with time by the development of tissue fibrosis. Several growth factors capable of improving muscle regeneration were investigated; basic fibroblast growth factor, insulin-like growth factor, and nerve growth factors were identified as substances capable of enhancing muscle regeneration and improving muscle force in the strained injured muscle. The current study should aid in the development of strategies to promote efficient muscle healing and complete recovery after strain injury.

L141 ANSWER 10 OF 83 MEDLINE
ACCESSION NUMBER: 2000158745 MEDLINE
DOCUMENT NUMBER: 20158745 PubMed ID: 10694204
TITLE: Vascular endothelial growth factor attenuates trauma-induced injury in rats.
AUTHOR: Campbell B; Chuhran C; Lefer A M
CORPORATE SOURCE: Department of Physiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA 19107-6799, USA.
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (2000 Jan) 129 (1) 71-6. Journal code: B00; 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000427
Last Updated on STN: 20000427
Entered Medline: 20000418

AB Endothelial dysfunction and loss of nitric oxide (NO) is an integral part of the initiation and maintenance of the inflammatory process such as that occurring in traumatic shock, and is considered responsible for much of the trauma induced microvascular injury. We investigated the effects of a vascular endothelial growth factor (VEGF) in a rat model of traumatic shock. Pentobarbital-anaesthetized rats subjected to Noble-Collip drum trauma developed a shock state characterized by marked hypotension and a 93% mortality rate with a mean survival time of 108+/-10 min in 14 rats. Accompanying these effects was a significant degree of endothelial dysfunction and a markedly elevated intestinal myeloperoxidase (MPO) activity. Treatment with 125 microg kg(-1) VEGF administered intravenously 18 h pre-trauma, increased survival rate to 67% ($P<0.01$), and prolonged survival time to 252+/-24 min in 12 rats ($P<0.01$). VEGF also significantly preserved the endothelium-dependent relaxation to ACh indicating a preservation of endothelium-derived NO. Our results indicate that endothelial dysfunction with its accompanying loss of NO plays an important role in tissue injury associated with trauma, and that preservation of NO is beneficial in traumatic shock. The mechanisms of the protective effect of VEGF in trauma involves preservation of eNOS function and diminished neutrophil accumulation resulting in reduced neutrophil-mediated tissue injury. British Journal of Pharmacology (2000) 129, 71 - 76

L141 ANSWER 11 OF 83 MEDLINE
ACCESSION NUMBER: 2000441192 MEDLINE
DOCUMENT NUMBER: 20385942 PubMed ID: 10929647
TITLE: [The role of growth factors in wound healing]. Die Rolle der Wachstumsfaktoren in der Wundheilung.
AUTHOR: Debus E S; Schmidt K; Ziegler U E; Thiede A
CORPORATE SOURCE: Chirurgische Universitatsklinik, Wurzburg..

sebastian.debus@mail.uni-wuerzburg.de
SOURCE: ZENTRALBLATT FUR CHIRURGIE, (2000) 125 Suppl 1 49-55. Ref: 76
Journal code: Y5I; 0413645. ISSN: 0044-409X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000921

AB Growth factors are mediators with essential importance for undisturbed repair process after wounding. The well coordinated concert of these substances is necessary for healing with complete restoration of function and morphology. These complex mechanisms are disturbed during secondary and delayed repair. The result is protracted healing course and inferior scar quality--either hypo- or hypertrophic. Local and systemic application of these growth factors seems to add important instruments for therapeutic use in the treatment of chronic wounds. Knowledge from experimental research is encouraging, although the exact mechanisms of synergistic action are not completely understood. However, the results from clinical use in controlled studies do not meet these expectations by far. The main reasons for this dilemma are thought to be little understanding in the complex interactions of these substances. In fact, different wound entities seem to reveal different cytokine profiles during the course of repair. Further intensive research therefore is required for the rational use of growth factors in the clinical setting.

L141 ANSWER 12 OF 83 MEDLINE
ACCESSION NUMBER: 1999116173 MEDLINE
DOCUMENT NUMBER: 99116173 PubMed ID: 9917648
TITLE: Potential role of fibroblast growth factor in enhancement of fracture healing.
AUTHOR: Radomsky M L; Thompson A Y; Spiro R C; Poser J W
CORPORATE SOURCE: Orquest Inc., Mountain View, CA 94043-5712, USA.
SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (1998 Oct) (355 Suppl) S283-93.
Journal code: DFY; 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 20000303
Entered Medline: 19990210

AB Fibroblast growth factors are present in significant amounts in bone and several studies have suggested that they may be involved in normal fracture healing. It is well established that fibroblast growth factors have mitogenic and angiogenic activity on mesoderm and neuroectoderm derived cells. Of particular interest as a member of the fibroblast growth factor family, basic fibroblast growth factor stimulates mitogenesis, chemotaxis, differentiation, and angiogenesis. It also plays an important role in the development of vascular, nervous, and skeletal systems, promotes the maintenance and survival of certain tissues, and stimulates wound healing and tissue repair. Animal studies have shown that the direct injection of fibroblast growth factor into fresh fractures stimulates callus formation, which provides mechanical stability to the fracture, accelerates healing, and restores competence. The matrix used to present the fibroblast growth factor at the fracture site plays a critical role in

the effectiveness of the treatment. The evaluation of injectable basic fibroblast growth factor in a sodium hyaluronate gel for its effectiveness in stimulating fracture healing is described. When applied directly into a freshly created fracture in the rabbit fibula, a single injection of the basic fibroblast growth factor and hyaluronan results in the stimulation of callus formation, increased bone formation, and earlier restoration of mechanical strength at the fracture site. The hyaluronan gel serves as a reservoir that sequesters the basic fibroblast growth factor at the injection site for the length of time necessary to create an environment conducive to fracture healing. It is concluded that basic fibroblast growth factor and sodium hyaluronate act synergistically to accelerate fracture healing and that the combination is suitable for clinical evaluation as a therapy in fracture treatment.

L141 ANSWER 13 OF 83 MEDLINE
ACCESSION NUMBER: 1998120354 MEDLINE
DOCUMENT NUMBER: 98120354 PubMed ID: 9458733
TITLE: Podokinesis in endothelial cell migration: role of nitric oxide.
AUTHOR: Noiri E; Lee E; Testa J; Quigley J; Colflesh D; Keese C R; Giaever I; Goligorsky M S
CORPORATE SOURCE: Department of Medicine, State University of New York, Stony Brook 11794-8152, USA.
CONTRACT NUMBER: DK-41573 (NIDDK)
DK-45695 (NIDDK)
DK-52783 (NIDDK)
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1998 Jan) 274 (1 Pt 1) C236-44.
Journal code: 3U8; 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 19980226
Entered Medline: 19980219

AB Previously, we demonstrated the role of nitric oxide (NO) in transforming epithelial cells from a stationary to locomoting phenotype [E. Noiri, T. Peresleni, N. Srivastava, P. Weber, W.F. Bahou, N. Peunova, and M. S. Goligorsky. Am. J. Physiol. 270 (Cell Physiol. 39): C794-C802, 1996] and its permissive function in endothelin-1-stimulated endothelial cell migration (E. Noiri, Y. Hu, W. F. Bahou; C. Keese, I. Giaever, and M. S. Goligorsky, J. Biol: Chem. 272: 1747-1753, 1997). In the present study, the role of functional NO synthase in executing the vascular endothelial growth factor (VEGF)-guided program of endothelial cell migration and angiogenesis was studied in two independent experimental settings. First, VEGF, shown to stimulate NO release from simian virus 40-immortalized microvascular endothelial cells, induced endothelial cell transwell migration, whereas NG-nitro-L-arginine methyl ester (L-NAME) or antisense oligonucleotides to endothelial NO synthase suppressed this effect of VEGF. Second, in a series of experiments on endothelial cell wound healing, the rate of VEGF-stimulated cell migration was significantly blunted by the inhibition of NO synthesis. To gain insight into the possible mode of NO action, we next addressed the possibility that NO modulates cell matrix adhesion by performing impedance analysis of endothelial cell monolayers subjected to NO. The data showed the presence of spontaneous fluctuations of the resistance in ostensibly stationary endothelial cells. Spontaneous oscillations were induced by NO, which also inhibited cell matrix adhesion. This process we propose to term "podokinesis" to emphasize a scalar from of micromotion that, in the presence of guidance cues, e.g., VEGF, is transformed to a vectorial movement. In conclusion, execution of the program for directional

endothelial cell migration requires two coexisting messages: NO-induced podokinesis (scalar motion) and guidance cues, e.g., VEGF, which imparts a vectorial component to the movement. Such a requirement for the dual signaling may explain a mismatch in the demand and supply with newly formed vessels in different pathological states accompanied by the inhibition of NO synthase.

L141 ANSWER 14 OF 83 MEDLINE
ACCESSION NUMBER: 1999366121 MEDLINE
DOCUMENT NUMBER: 99366121 PubMed ID: 10437068
TITLE: Basic fibroblast growth factor (bFGF) and wound healing: a multi-centers and controlled clinical trial in 1024 cases.
AUTHOR: Fu X; Shen Z; Chen Y
CORPORATE SOURCE: The 304th Hospital of PLA, Beijing, P.R. China.
SOURCE: CHUNG-KUO HSIU FU CHUNG CHIEN WAI KO TSA CHIH [CHINESSE JOURNAL OF REPARATIVE AND RECONSTRUCTIVE SURGERY], (1998 Jul) 12 (4) 209-11.
Journal code: CNP; 9425194. ISSN: 1002-1892.
PUB. COUNTRY: China
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE III)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991103

AB To evaluate the effects of bFGF on wound healing and the side-effects of bFGF, a multi-centers and controlled clinical trial were carried out in 32 hospitals in China. One thousand and twenty-four cases with acute wounds such as burn, donor site or operative wound and chronic wounds such as bed sore, draining sinus, ulcer were treated with bFGF. Another 826 cases with the similar wounds were used as control. The results showed: 1. The duration of wound healing was shorted 3-4 days in trial group when compared with the contorl; 2. The successful rates from bFGF on promoting the wound healing for burns, operative wounds and chronic dermal ulcers was 95.2%, 96.5% and 93.5%, respectively; 3. No adverse reaction was found. CONCLUSION: 1. bEGF can make the "silent" reparative cells dividing and proliferating. 2. bFGF can improve the quality and the velocity of wound healing.

L141 ANSWER 15 OF 83 MEDLINE
ACCESSION NUMBER: 97085813 MEDLINE
DOCUMENT NUMBER: 97085813 PubMed ID: 8931898
TITLE: Enhanced angiogenesis and granulation tissue formation by basic fibroblast growth factor in healing-impaired animals.
AUTHOR: Okumura M; Okuda T; Okamoto T; Nakamura T; Yajima M
CORPORATE SOURCE: Pharmacology Laboratories, Kaken Pharmaceutical Co., Ltd., Kyoto, Japan.
SOURCE: ARZNEIMITTEL-FORSCHUNG, (1996 Oct) 46 (10) 1021-6.
Journal code: 91U; 0372660. ISSN: 0004-4172.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970113

AB The effect of basic fibroblast growth factor (bFGF) on angiogenesis and granulation tissue formation in normal and healing-impaired animals was

studied. bFGF showed a dose-dependent enhancement of granulation tissue formation in the subcutaneous implantation of a paper disk in normal rats. Application of bFGF restored the formation in healing-impaired rat models treated with steroid, chemotherapy and X-ray irradiation. The angiogenic activity of bFGF was also demonstrated in the micro-pocket assay using the cornea of rabbits. Repeated applications of bFGF accelerated closure of full-thickness excisional wounds in diabetic mice, but the high doses showed rather diminished response. In contrast histological and gross evaluation of wound tissues revealed enhanced angiogenesis and granulation tissue formation in a dose-dependent manner. The findings suggested that the topical application of excess amounts of bFGF might reduce its ability to promote wound closure because of the prolonged responses in both neovascular and granulation tissue formation.

L141 ANSWER 16 OF 83 MEDLINE
ACCESSION NUMBER: 96223584 MEDLINE
DOCUMENT NUMBER: 96223584 PubMed ID: 8659931
TITLE: Vascular effects of sustained-release fibroblast growth factors.
AUTHOR: Hom D B; Medhi K; Assefa G; Juhn S K; Johnston T P
CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, University of Minnesota School of Medicine, Minneapolis 55455, USA.
SOURCE: ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, (1996 Feb) 105 (2) 109-16.
Journal code: 5Q2; 0407300. ISSN: 0003-4894.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960808
Last Updated on STN: 19960808
Entered Medline: 19960801

AB Since the half-life of most angiogenic growth factors is several hours or less, sustained-release delivery would be optimal for their future clinical use. Two fibroblast growth factors, basic fibroblast growth factor (bFGF) and endothelial cell growth factor (ECGF), were delivered in two sustained-released modalities (poloxamer 407 and a gelatin sponge [Gelfoam]) to attempt to increase soft tissue vascularity. In vitro bioactivity of ECGF-poloxamer formulations was also tested on endothelial cell cultures. Among vascular-compromised skin flaps in rabbits, ECGF-poloxamer (N = 26), bFGF-poloxamer (N = 5), ECGF-poloxamer (N = 9, irradiated), and bFGF-Gelfoam flaps (N = 22) did not demonstrate significant differences in viability and vascularity compared to controls ($p > .05$). Irradiation had a detrimental effect on both flap vascularity and viability ($p = .02$). Future efforts for sustained delivery of angiogenic proteins are critical in order to make them clinically useful in wound healing.

L141 ANSWER 17 OF 83 MEDLINE
ACCESSION NUMBER: 95160697 MEDLINE
DOCUMENT NUMBER: 95160697 PubMed ID: 7857288
TITLE: Vascular endothelial growth factor causes endothelial proliferation after vascular injury.
AUTHOR: Burke P A; Lehmann-Bruinsma K; Powell J S
CORPORATE SOURCE: Department of Medicine, University of California at Davis.
CONTRACT NUMBER: T32HL076 (NHLBI)
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995 Feb 6) 207 (1) 348-54.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950314

AB Vascular endothelial growth factor was infused into rat carotid arteries for 3 minutes immediately after endothelial denudation by balloon injury. Endothelial proliferation was determined by immunohistochemical labelling of proliferating cell nuclear antigen using Hautchen preparations. The proliferation index, or number of proliferating cells/total cells, measured at 25.5 or 30 hours was markedly increased after infusion of vascular endothelial growth factor. In addition, the total number of proliferating cells increased with increasing doses up to 100 micrograms total dose per infusion. These data indicate that infusion of vascular endothelial growth factor increases endothelial cell proliferation after mechanical denudation injury of the vascular wall.

L141 ANSWER 18 OF 83 MEDLINE
ACCESSION NUMBER: 96296520 MEDLINE
DOCUMENT NUMBER: 96296520 PubMed ID: 8697247
TITLE: A study on the factors influencing bFGF to improve wound healing in severe burn.
AUTHOR: Zheng J; Wang S; Yan D
CORPORATE SOURCE: Zhujiang Hospital, First Military Medical College, Guangzhou.
SOURCE: CHUNG-HUA CHENG HSING SHAO SHANG WAI KO TSA CHIH [CHINESE JOURNAL OF PLASTIC SURGERY AND BURNS], (1995 Sep) 11 (5) 343-5.
Journal code: CHI; 8510296. ISSN: 1000-7806.
PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960912
Last Updated on STN: 19960912
Entered Medline: 19960903

AB The factors influencing basic fibroblast growth factor (bFGF) to improve wound healing in severe burn were studied. Rats were subjected to 15% III degrees burn. The results showed that high activity of bFGF was maintained after escharectomy in early period. In treated group 84.0% of rats wound healing was observed on the 40th day, while it was 9.0% in control group. Heparin could enhance activity of bFGF to stimulate formation of granulation tissue, regeneration of capillary, proliferation of fibroblast and DNA synthesis. Control of infection was beneficial to preserve activity of bFGF. The authors believe that the proper time to use bFGF is one week after injury.

L141 ANSWER 19 OF 83 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:53422 CAPLUS
DOCUMENT NUMBER: 132:73673
TITLE: **Component B** as **angiogenic agent** in combination with human growth factors
INVENTOR(S): Ziche, Marina; Donini, Silvia; Borrelli, Francesco
PATENT ASSIGNEE(S): Applied Research Systems ARS Holding N.V., Neth. Antilles
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002579	A2	20000120	WO 1999-EP4605	19990702
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9950306	A1	20000201	AU 1999-50306	19990702
EP 1093380	A2	20010425	EP 1999-934563	19990702
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001031733	A1	20011018	US 2001-756185	20010109

PRIORITY APPLN. INFO.: EP 1998-112775 A 19980709
WO 1999-EP4605 W 19990702

AB The present invention refers to the use of **Component B** (81-residue protein originally isolated from human urine) as **angiogenic agent** in combination with human growth factors.

IT **106096-93-9, Basic fibroblast** growth factor
127464-60-2, Vascular endothelial growth factor
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**component B** as **angiogenic agent** in combination with human growth factors)

L141 ANSWER 20 OF 83 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
ACCESSION NUMBER: 1999:492671 CAPLUS
DOCUMENT NUMBER: 131:284627
TITLE: Growth factors in gastrointestinal diseases
AUTHOR(S): Szabo, Sandor; Gombos, Zoltan; Sandor, Zsuzsa
CORPORATE SOURCE: Departments of Pathology and Pharmacology, Irvine Experimental Pathology & Pharmacology Laboratory, Pathology & Laboratory Medicine Service, VA Medical Center, University of California, Long Beach, CA, USA
SOURCE: BioDrugs (1999), 12(1), 27-41
CODEN: BIDRF4; ISSN: 1173-8804
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 113 refs., which focuses on the recent investigations demonstrating a pharmacol. and pathophysiol. role for basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF) and vascular endothelial growth factor (**VEGF**) in ulcerative and inflammatory lesions in the upper and lower gastrointestinal (GI) tract. Our initial expts. revealed that intragastric administration of bFGF-w, acid-resistant bFGF-CS23 and PDGF-BB healed chronic cysteamine (mercaptamine)-induced duodenal ulcer in rats, without decreasing gastric acid secretion or concn. Subsequently we and others have demonstrated that these peptides accelerate the healing of chronic gastric ulcers, chronic erosive gastritis and ulcerative colitis although they have no or modest acute gastric protective activity. Our recent results revealed a decreased bioactivity of bFGF and PDGF in the presence of certain strains of Helicobacter pylori, and this might explain, at least in part, the poor rates of ulcer healing in H. pylori-pos. patients. **VEGF**, in addn. to stimulating angiogenesis and granulation tissue prodn. in duodenal ulcer healing, also has an acute gastroprotective effect. New

biochem., mol. biol. and immunohistochem. studies indicate that bFGF, PDGF and **VEGF** play a pathophysiol. role in the natural history of ulcer healing. Thus, growth factor research, esp. regarding their possible use as a therapeutic tool in duodenal ulcer and colitis, is challenging. On the other hand, in some GI malignancies the diagnostic use of bFGF might be of clin. benefit. However, much research work is needed to transform these "endogenous drugs" to "diagnostic tools" and "exogenous drugs".

IT **106096-93-9, Basic fibroblast** growth factor
127464-60-2, Vascular endothelial growth factor
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BIOL (Biological study); PROC (Process)
(**bFGF**, PDGF and **VEGF** pharmacol. and pathophysiol. role in gastrointestinal disease and healing)

REFERENCE COUNT: 113
REFERENCE(S):
(1) Antoniades, H; Science 1983, V220, P963 CAPLUS
(4) Basilico, C; Adv Cancer Res 1992, V59, P115 CAPLUS
(5) Betsholtz, C; Nature 1986, V320, P695 CAPLUS
(7) Chait, A; Proc Nat Acad Sci U S A 1980, V77, P4084 CAPLUS
(8) de Vries, C; Science 1992, V255, P989 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 21 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:713092 CAPLUS
DOCUMENT NUMBER: 135:268268
TITLE: Human and mouse **VEGF**-modulated genes, protein and cDNA sequences and uses in modulating angiogenesis and apoptosis
INVENTOR(S): Rastelli, Luca K.; Gerber, Hans-Peter
PATENT ASSIGNEE(S): Curagen Corporation, USA; Genentech, Inc.
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070174	A2	20010927	WO 2001-US9043	20010321

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-191201 P 20000321

AB The present invention provides methods for modulating angiogenesis and/or apoptosis comprising modulating the activity of at least one **VEGF**-modulated gene polypeptide. The invention also provides pharmaceutical compns. for modulating angiogenesis and apoptosis for the prevention or treatment of diseases assocd. with **VEGF**-modulated genes expression. The invention also provides diagnostic assays that use **VEGF**-modulated gene polynucleotides that hybridize with naturally occurring sequences encoding **VEGF**-modulated genes and antibodies that specifically bind to the protein. The invention also provides novel human and mouse arginine-rich proteins (ARPs) and nucleotide sequences. The invention provides for genetically engineered expression vectors and

host cells comprising the nucleic acid sequence encoding ARPs and for a method for producing the protein.

IT **106096-93-9, Basic fibroblast** growth factor
127464-60-2, Vascular endothelial growth factor
RL: **BAC (Biological activity or effector, except adverse)**; BIOL (Biological study)
(human and mouse **VEGF**-modulated genes, differential gene expression in human umbilical cord endothelial cells treated with growth factors)

L141 ANSWER 22 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:545508 CAPLUS
DOCUMENT NUMBER: 135:132464
TITLE: Cyclic peptide inhibitors of VEGF, VEGF-C, and VEGF-D, preparation methods, pharmaceutical compositions, and therapeutic use
INVENTOR(S): Achen, Marc G.; Hughes, Richard A.; Stacker, Steven; Cendron, Angela
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052875	A1	20010726	WO 2001-US1533	20010118

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-176293 P 20000118
US 2000-204590 P 20000516

AB The invention provides monomeric monocyclic peptide inhibitors and dimeric bicyclic peptide inhibitors based on exposed loop fragments of a growth factor protein, e.g. loop 1, loop 2 or loop 3 of VEGF-D, as well as methods of making them, pharmaceutical compns. contg. them, and therapeutic methods of use.

REFERENCE COUNT: 3
REFERENCE(S):
(1) Children's Medical Center Corporation; WO 99/29861 A1 1999 CAPLUS
(2) Jia; Biochem Biophys Res Comm 2001, V283, P164 CAPLUS
(3) Piossek; J Biol Chem 1999, V274(9), P5612 CAPLUS

L141 ANSWER 23 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:310080 CAPLUS
DOCUMENT NUMBER: 135:116756
TITLE: The antiangiogenic property of docetaxel is synergistic with a recombinant humanized monoclonal antibody against **vascular endothelial growth factor** or 2-methoxyestradiol but antagonized by endothelial growth factors
AUTHOR(S): Sweeney, Christopher J.; Miller, Kathy D.; Sissons,

Sean E.; Nozaki, Shinichi; Heilman, Douglas K.; Shen, Jianzhao; Sledge, George W., Jr.

CORPORATE SOURCE: Department of Medicine, Indiana University, Indianapolis, IN, 46202, USA

SOURCE: Cancer Res. (2001), 61(8), 3369-3372
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Numerous chemotherapeutic agents have been shown to have an inhibitory effect on endothelial cell proliferation and migration, and tubule formation. In this study, we examd. the antiangiogenic activity of docetaxel. Docetaxel inhibited endothelial cell proliferation and tubule formation in vitro in a dose-dependent fashion. Docetaxel treatment also inhibited angiogenesis in an in vivo Matrigel plug assay. The endothelial stimulating factors, vascular endothelial cell growth factor (**VEGF**) and basic fibroblast growth factor are able to protect endothelial cells from the antiangiogenic properties of docetaxel. This protective effect can be overcome by a recombinant humanized monoclonal antibody directed against **VEGF** in both in vitro and in vivo models. Similarly, combination of docetaxel with the antiangiogenic agent 2-methoxyestradiol also overcomes the protective effect of **VEGF** in both in vitro and in vivo models. These data suggest that microenvironmental factors (e.g., local release of **VEGF** and basic fibroblast growth factor) could play a role in decreasing the antiangiogenic effects of docetaxel, whereas agents such as 2-methoxyestradiol and recombinant humanized monoclonal antibody directed against **VEGF** may reverse this protective effect.

IT **106096-93-9, Basic fibroblast** growth factor
127464-60-2, Vascular endothelial growth factor
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(antiangiogenic property of docetaxel is synergistic with a humanized MAb against **vascular endothelial growth factor** or 2-methoxyestradiol but antagonized by endothelial growth factors)

REFERENCE COUNT: 24
REFERENCE(S):
(1) Belotti, D; Clin Cancer Res 1996, V2, P1843 CAPLUS
(2) Browder, T; Cancer Res 2000, V60, P1878 CAPLUS
(3) Bruno, R; J Clin Oncol 1998, V16, P187 CAPLUS
(4) Chou, T; Adv Enzyme Regul 1984, V22, P27 CAPLUS
(5) Fennelly, D; J Clin Oncol 1997, V15, P187 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 24 OF 83 CAPLUS
ACCESSION NUMBER: 2001:135858 CAPLUS
DOCUMENT NUMBER: 135:189849
TITLE: Phase Ib trial of intravenous recombinant humanized monoclonal antibody to vascular endothelial growth factor in combination with chemotherapy in patients with advanced cancer: Pharmacologic and long-term safety data

AUTHOR(S): Margolin, K.; Gordon, M. S.; Holmgren, E.; Gaudreault, J.; Novotny, W.; Fyfe, G.; Adelman, D.; Stalter, S.; Breed, J.

CORPORATE SOURCE: Department of Medical Oncology and Therapeutics Research, City of Hope National Cancer Center, Duarte, CA, 91010, USA

SOURCE: J. Clin. Oncol. (2001), 19(3), 851-856
CODEN: JCONDN; ISSN: 0732-183X

PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tumor angiogenesis mediated by vascular endothelial growth factor (VEGF) is inhibited by the recombinant humanized (rhu) monoclonal antibody (MAb) rhuMAbVEGF, which has synergy with chemotherapy in animal models. The present study was designed to assess the safety and pharmacokinetics of weekly i.v. (IV) rhuMAbVEGF with one of three std. chemotherapy regimens. Twelve adult patients were enrolled four on each combination. RhuMAbVEGF, 3 mg/kg IV, was administered weekly for 8 wk with (1) doxorubicin 50 mg/m2 every 4 wk; (2) carboplatin at area under the curve of 6 plus paclitaxel 175 mg/m2 every 4 wk; and (3) fluorouracil (5-FU) 500 mg/m2 with leucovorin 20 mg/m2 weekly, weeks 1 to 6 every 8 wk. The median no. of rhuMAbVEGF doses delivered was eight (range, four to eight doses). Grade 3 toxicities were diarrhea (one 5-FU patient), thrombocytopenia (two patients on carboplatin plus paclitaxel), and leukopenia (one patient on carboplatin plus paclitaxel). These toxicities were likely attributable to the chemotherapy component of the regimen. The mean (.+-. SD) peak serum level of rhuMAbVEGF was 167 .+-. 46 .mu.g/mL, and the mean terminal half-life was 13 days. Total (free plus bound) serum VEGF levels increased from 51 .+-. 39 pg/mL (day 0) to 211 .+-. 112 (day 49) pg/mL. Three responding patients continued treatment with rhuMAbVEGF and chemotherapy, receiving the equiv. of 36, 20, and 40 total rhuMAbVEGF doses with no cumulative or late toxicities. RhuMAbVEGF can be safely combined with chemotherapy at doses assocd. with VEGF blockade and without apparent synergistic toxicity. Its contribution to the treatment of advanced solid tumors should be evaluated in randomized treatment trials.

IT **127464-60-2, Vascular endothelial growth factor**
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antitumor activity of i.v. recombinant humanized monoclonal antibody to **vascular endothelial growth factor** in combination with chemotherapy in patients with advanced cancer)

REFERENCE COUNT: 25
REFERENCE(S):
(1) Bergers, G; Science 1999, V284, P808 CAPLUS
(2) Boehm, T; Nature 1997, V390, P404 CAPLUS
(3) Borgstrom, P; Anticancer Res 1999, V19, P4203 CAPLUS
(7) Ferrara, N; Endocrine Rev 1992, V13, P18 CAPLUS
(11) Gnarra, J; Proc Natl Acad Sci USA 1996, V93, P10589 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 25 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:309865 CAPLUS
DOCUMENT NUMBER: 135:91393
TITLE: Gene transfer of antisense hypoxia inducible factor-1 .alpha. enhances the therapeutic efficacy of cancer immunotherapy
AUTHOR(S): Sun, X.; Kanwar, J. R.; Leung, E.; Lehnert, K.; Wang, D.; Krissansen, G. W.
CORPORATE SOURCE: Division of Molecular Medicine, Faculty of Medicine and Health Science, University of Auckland, Auckland, N. Z.
SOURCE: Gene Ther. (2001), 8(8), 638-645
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Solid tumors meet their demands for nascent blood vessels and increased glycolysis, to combat hypoxia, by activating multiple genes involved in angiogenesis and glucose metab. Hypoxia inducible factor-1 (HIF-1) is a constitutively expressed basic helix-loop-helix transcription factor, formed by the assembly of HIF-1.alpha. and HIF-1.beta. (Arnt), that is

stabilized in response to hypoxia, and rapidly degraded under normoxic conditions. It activates the transcription of genes important for maintaining oxygen homeostasis. Here, we demonstrate that engineered down-regulation of HIF-1.alpha. by intratumoral gene transfer of an antisense HIF-1.alpha. plasmid leads to the down-regulation of **VEGF**, and decreased tumor microvessel d. Antisense HIF-1.alpha. monotherapy resulted in the complete and permanent rejection of small (0.1 cm in diam.) EL-4 tumors, which is unusual for an anti-**angiogenic agent** where transient suppression of tumor growth is the norm. It induced NK cell-dependent rejection of tumors, but failed to stimulate systemic T cell-mediated anti-tumor immunity, and **synergized** with B7-1-mediated immunotherapy to cause the NK cell and CD8 T cell-dependent rejection of larger EL-4 tumors (0.4 cm in diam.) that were refractory to monotherapies. Mice cured of their tumors by combination therapy resisted a rechallenge with parental tumor cells, indicating systemic antitumor immunity had been achieved. In summary, while intensive investigations are in progress to target the many HIF-1 effectors, the results herein indicate that blocking hypoxia-inducible pathways and enhancing NK-mediated antitumor immunity by targeting HIF-1 itself may be advantageous, esp. when combined with cancer immunotherapy.

IT **127464-60-2, Vascular endothelial growth factor**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(gene transfer of antisense hypoxia inducible factor-1 .alpha. enhances the therapeutic efficacy of cancer immunotherapy and inhibition of)

REFERENCE COUNT: 44
REFERENCE(S):
(1) Baguley, B; BioDrugs 1997, V8, P119 CAPLUS
(2) Blancher, C; Cancer Metast Rev 1998, V17, P187 CAPLUS
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(6) Bunn, H; Physiol Rev 1996, V76, P839 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 26 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:342789 CAPLUS
DOCUMENT NUMBER: 135:91047
TITLE: Synergism between **vascular endothelial growth factor** and placental growth factor contributes to angiogenesis and plasma extravasation in pathological conditions
AUTHOR(S): Carmeliet, Peter; Moons, Lieve; Luttun, Aernout; Vincenti, Valeria; Compernolle, Veerle; De Mol, Maria; Wu, Yan; Bono, Francoise; Devy, Laetitia; Beck, Heike; Scholz, Dimitri; Acker, Till; DiPalma, Tina; Dewerchin, Mieke; Noel, Agnes; Stalmans, Ingeborg; Barra, Adriano; Blacher, Sylvia; Vandendriessche, Thierry; Ponten, Annica; Eriksson, Ulf; Plate, Karl H.; Foidart, Jean-Michel; Schaper, Wolfgang; Charnock-Jones, D. Stephen; Hicklin, Daniel J.; Herbert, Jean-Marc; Collen, Desire; Persico, M. Graziella
CORPORATE SOURCE: The Center for Transgene Technology and Gene Therapy, Flanders Interuniversity Institute for Biotechnology, KU Leuven, Louvain, Belg.
SOURCE: Nat. Med. (N. Y., NY, U. S.) (2001), 7(5), 575-583
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Vascular endothelial growth factor (**VEGF**) stimulates angiogenesis by activating **VEGF** receptor-2 (VEGFR-2). The role

of its homolog, placental growth factor (PIGF), remains unknown. Both **VEGF** and PIGF bind to **VEGF** receptor-1 (VEGFR-1), but it is unknown whether VEGFR-1, which exists as a sol. or a membrane-bound type, is an inert decoy or a signaling receptor for PIGF during angiogenesis. Here, we report that embryonic angiogenesis in mice was not affected by deficiency of PIGF (Pgf-/-). **VEGF**-B, another ligand of VEGFR-1, did not rescue development in Pgf-/- mice. However, loss of PIGF impaired angiogenesis, plasma extravasation and collateral growth during ischemia, inflammation, wound healing and cancer. Transplantation of wild-type bone marrow rescued the impaired angiogenesis and collateral growth in Pgf-/- mice, indicating that PIGF might have contributed to vessel growth in the adult by mobilizing bone-marrow-derived cells. The synergism between PIGF and **VEGF** was specific, as PIGF deficiency impaired the response to **VEGF**, but not to bFGF or histamine. VEGFR-1 was activated by PIGF, given that anti-VEGFR-1 antibodies and a Src-kinase inhibitor blocked the endothelial response to PIGF or **VEGF**/PIGF. By upregulating PIGF and the signaling subtype of VEGFR-1, endothelial cells amplify their responsiveness to **VEGF** during the "angiogenic switch" in many pathol. disorders.

IT **127464-60-2, Vascular endothelial growth factor**
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**VEGF** and placental growth factor synergism contributes to angiogenesis and plasma extravasation in pathol. conditions)

IT **106096-93-9, Basic fibroblast** growth factor
RL: **BAC (Biological activity or effector, except adverse)**; BIOL (Biological study)
(**VEGF** and placental growth factor synergism contributes to angiogenesis and plasma extravasation in pathol. conditions)

REFERENCE COUNT: 45
REFERENCE(S):
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(4) Cao, Y; J Clin Invest 1996, V98, P2507 CAPLUS
(5) Carmeliet, P; Cell 1999, V98, P147 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 27 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:248765 CAPLUS
DOCUMENT NUMBER: 135:656
TITLE: Effect of FGF-1 and FGF-2 on **VEGF** binding to human umbilical vein endothelial cells
AUTHOR(S): Chen, Jun-Hui; Wang, Xin-Chang; Kan, Mikio; Sato, J. Denry
CORPORATE SOURCE: Pharmaceutic Biotechnology Key Laboratory, Department of Biochemistry, Nanjing University, Nanjing, 210093, Peop. Rep. China
SOURCE: Cell Biol. Int. (2001), 25(3), 257-260
CODEN: CBIIEV; ISSN: 1065-6995
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB When FGF-1 or FGF-2 and **VEGF** were added together, the mitogenic effect of FGF-1 or FGF-2 and **VEGF** on HUVEC was additive. However, when HUVECs were preincubated for 2 days with 10 ng/mL FGF-1 in the absence of **VEGF**, the Scatchard plot of [125I]**VEGF** binding sites was shifted to the right: both affinity classes of **VEGF** binding sites were equally affected, such that the total no. of sites increased two-fold. It is suggested that this type of interaction may be related to tumor angiogenesis and wound repair. (c)

2001 Academic Press.
IT **106096-93-9**, FGF 2
RL: **BAC (Biological activity or effector, except adverse)**; BIOL (Biological study)
(FGF-1 and FGF-2 effect on **VEGF** binding to human umbilical vein endothelial cells)
IT **127464-60-2**, **Vascular endothelial growth factor**
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BIOL (Biological study); PROC (Process)
(FGF-1 and FGF-2 effect on **VEGF** binding to human umbilical vein endothelial cells)
REFERENCE COUNT: 12
REFERENCE(S):
(1) Campbell, C; Int J Cancer 1999, V80, P868 CAPLUS
(2) Conn, G; Proc Natl Acad Sci USA 1990, V87, P1323 CAPLUS
(3) Connolly, D; J Biol Chem 1989, V264, P20017 CAPLUS
(5) Detmar, M; Am J Pathol 2000, V156, P159 CAPLUS
(6) Ferrara, N; Biochem Biophys Res Commun 1989, V161, P851 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 28 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:467666 CAPLUS
DOCUMENT NUMBER: 135:298710
TITLE: Upregulation of oxidant-induced VEGF expression in cultured keratinocytes by a grape seed proanthocyanidin extract
AUTHOR(S): Khanna, S.; Roy, S.; Bagchi, D.; Bagchi, M.; Sen, C. K.
CORPORATE SOURCE: Department of Surgery, Laboratory of Molecular Medicine, The Ohio State University Medical Center, Columbus, OH, USA
SOURCE: Free Radical Biol. Med. (2001), 31(1), 38-42
CODEN: FRBMEH; ISSN: 0891-5849
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Angiogenesis plays a central role in wound healing. Among many known growth factors, vascular endothelial growth factor (VEGF) is believed to be the most prevalent, efficacious, and long-term signal that is known to stimulate angiogenesis in wounds. The wound site is rich in oxidants such as hydrogen peroxide mostly contributed by neutrophils and macrophages. Proanthocyanidins or condensed tannins are a group of biol. active polyphenolic bioflavonoids that are synthesized by many plants. This study provides first evidence showing that natural exts. such as grape seed proanthocyanidin ext. contg. 5000 ppm resveratrol (GSPE) facilitates oxidant-induced VEGF expression in keratinocytes. Using a RNase protection assay (RPA), the ability of GSPE to regulate oxidant-induced changes in several angiogenesis-related genes were studied. While mRNA responses were studied using RPA, VEGF protein release from cells to the culture medium was studied using ELISA. Pretreatment of HaCaT keratinocytes with GSPE upregulated both hydrogen peroxide as well as TNF-.alpha.-induced VEGF expression and release. The current results suggest that GSPE may have beneficial therapeutic effects in promoting dermal wound healing and other related skin disorders.
REFERENCE COUNT: 24
REFERENCE(S):
(1) Babior, B; N Engl J Med 1978, V298, P659 CAPLUS
(2) Bagchi, D; Gen Pharmacol 1998, V30, P771 CAPLUS
(3) Bagchi, D; Res Commun Mol Pathol Pharmacol 1997, V95, P179 CAPLUS
(4) Bagchi, M; Free Radic Biol Med 1999, V26, P992 CAPLUS

(6) Boukamp, P; J Cell Biol 1988, V106, P761 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 29 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:314562 CAPLUS
DOCUMENT NUMBER: 132:329936
TITLE: Vascular endothelial growth factor-like protein from orf virus NZ2 binds and activates mammalian VEGF receptor-2
INVENTOR(S): Wise, Lyn M.; Mercer, Andrew A.; Savory, Loreen J.; Fleming, Stephen B.; Stacker, Steven A.
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA; University of Otago
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025805	A1	20000511	WO 1999-US25869	19991102
W: AU, JP, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1126863	A1	20010829	EP 1999-958757	19991102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:
US 1998-106689 P 19981102
US 1998-106800 P 19981103
WO 1999-US25869 W 19991102

AB The invention is based on the discovery that a viral VEGF-like protein from the orf virus strain NZ2 and from the orf virus strain NZ10 is capable of binding to the extracellular domain of the VEGF receptor-2 to form bioactive complexes which mediate useful cellular responses and/or antagonize undesired biol. activities. Disclosed are methods which stimulate or inhibit these biol. activities, methods for therapeutic applications and antagonists of ORFV2-VEGF and/or NZ10.

IT **127464-60-2, Vascular endothelial growth factor**
RL: **BAC (Biological activity or effector, except adverse); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ORFV2 and NZ10 analogs; **vascular endothelial growth factor**-like protein from ORF virus NZ2 binds and activates mammalian **VEGF** receptor-2)

REFERENCE COUNT: 4
REFERENCE(S):
(1) Bayer Aktiengesellschaft; WO 9732029 A1 1997 CAPLUS
(2) Haig, D; Vet Res 1998, V29, P311 CAPLUS
(3) Lyttle, D; J Virology 1994, V68(1), P84 CAPLUS
(4) Max-Plank Gesellschaft Zur Forderung der Wissenschaften E V; WO 9950290 A1 1999 CAPLUS

L141 ANSWER 30 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:885954 CAPLUS
DOCUMENT NUMBER: 135:70864
TITLE: Effects of combinations of anti-rheumatic drugs on the production of **vascular endothelial growth factor** and **basic fibroblast** growth factor in cultured synoviocytes and patients with rheumatoid arthritis
AUTHOR(S): Nagashima, M.; Wauke, K.; Hirano, D.; Ishigami, S.;

Aono, H.; Takai, M.; Sasano, M.; Yoshino, S.
CORPORATE SOURCE: Department of Joint Disease and Rheumatism, Nippon Medical School, Sendagi, 113-8603, Japan
SOURCE: Rheumatology (Oxford) (2000), 39(11), 1255-1262
CODEN: RUMAFK; ISSN: 1462-0324
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To examine whether different combinations of disease-modifying anti-rheumatic drugs (DMARDs), including bucillamine (BUC), gold sodium thiomalate (GST), methotrexate (MTX), salazosulfapyridine (SASP) and dexamethasone (DEX; a steroid), act by inhibiting the prodn. of vascular endothelial growth factor (**VEGF**) and basic fibroblast growth factor (bFGF) in cultured synoviocytes, causing a decrease in their serum concns. in patients with rheumatoid arthritis (RA). The **VEGF** and bFGF concns. in cultured synoviocytes and peripheral blood from patients with RA were measured by ELISA and their serum concns. were measured at two time points. BUC and GST inhibited **VEGF** prodn. even when given alone, and a combination of BUC, GST and MTX with DEX also inhibited **VEGF** prodn. None of the DMARDs or DEX inhibited bFGF prodn. when given alone, but a combination of SASP and GST inhibited the prodn. of bFGF in cultured synoviocytes. Serum **VEGF** concns. were significantly decreased 6 mo after the commencement of medication compared with their concns. before medication. Our results show that the effects of a combination of DEX with any two of BUC, GST, SASP and MTX on the prodn. of **VEGF** and bFGF in cultured synoviocytes and on the serum concns. of **VEGF** in patients with RA may be based on synergistic or additive effects of the drugs.
IT **106096-93-9, Basic fibroblast** growth factor
127464-60-2, Vascular endothelial growth factor
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(effects of combinations of anti-rheumatic drugs on prodn. of **vascular endothelial growth factor** and **basic fibroblast** growth factor in cultured synoviocytes and human patients with rheumatoid arthritis)
REFERENCE COUNT: 47
REFERENCE(S):
(2) Aono, H; J Rheumatol 1996, V23, P65 CAPLUS
(4) Brody, M; Eur J Clin Chem Clin Biochem 1993, V31, P667 CAPLUS
(6) Carlin, G; Ann Rheum Dis 1992, V51, P1230 CAPLUS
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(10) Cronstein, B; Arthritis Rheum 1995, V38, P1040 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 31 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:191623 CAPLUS
DOCUMENT NUMBER: 133:103214
TITLE: Modulation of a fibrotic process induced by transforming growth factor beta-1 in dermal equivalents
AUTHOR(S): Gentilhomme, E.; Neveux, Y.; Lebeau, J.; Desmouliere, A.; Bergier, J.; Schmitt, D.; Haftek, M.
CORPORATE SOURCE: CRSSA, La Tronche, Fr.
SOURCE: Cell Biol. Toxicol. (2000), Volume Date 1999, 15(4), 229-238
CODEN: CBTOE2; ISSN: 0742-2091
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Why initially normal wound healing sometimes shifts toward an impaired

cicatrization is poorly understood. Collagen gels with incorporated fibroblasts constitute valuable in vitro models to study mechanisms of connective tissue reorganization. Such 1-wk-old, partially contracted normal dermal equiv. were treated with concns. of TGF-.beta.1 ranging from 1 to 10 ng/mL. The cytokine was applied in a single dose or four times at regular intervals, over a 2-wk period. Dose-dependent activation of fibroblasts was obsd. after treatment. The cytokine induced a myofibroblastic transformation of dermal cells, enhanced the process of dermal contraction, and stimulated synthesis of such proteins as cellular fibronectin, tenascin and smooth-muscle actin. This approach is more informative than models using pathol. or pretreated dermal cells, since it demonstrates newly induced modulation of fibrotic transformation in an initially normal dermal equiv. This in vitro assay will enable the study of mechanisms involved in the shift between normal and impaired fibrotic transformation during wound healing.

REFERENCE COUNT: 41

REFERENCE(S):
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(5) Cotton, S; J Pathol 1998, V184, P4 CAPLUS
(6) Desmouliere, A; Cell Biol 1995, V19, P471 CAPLUS
(7) Desmouliere, A; J Cell Biol 1993, V122, P103 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 32 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:413278 CAPLUS

DOCUMENT NUMBER: 133:329267

TITLE: Interaction of **angiogenesis** inhibitor TNP-470 with basic fibroblast growth factor receptors

AUTHOR(S): Bond, Sheldon J.; Klein, Scott A.; Anderson, Gary L.; Wittliff, James L.

CORPORATE SOURCE: Department of Surgery, Division of Pediatric Surgery, University of Louisville School of Medicine, Louisville, KY, 40202, USA

SOURCE: J. Surg. Res. (2000), 92(1), 18-22
CODEN: JSGRA2; ISSN: 0022-4804

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB TNP-470 is a synthetic analog of fumagillin that acts as a potent angiogenesis inhibitor. Recently, the authors lab. demonstrated that systemic administration of TNP-470 (5.0 mg/kg) decreased the rate of cutaneous wound healing by > 20%. In this study, the authors tested the hypothesis that TNP-470 interferes with the wound repair-stimulating action of basic fibroblast growth factor (bFGF) by competing with endogenous bFGF for its binding sites on the receptor protein. The influence of TNP-470 was examd. in vitro in a ligand competition assay of high- and low-affinity receptor binding to 125I-bFGF in NIH/3T3 cells. Results demonstrated that recognition of 125I-bFGF by low-affinity growth factor binding sites was decreased in the presence of TNP-470. However, TNP-470 inhibition of radiolabeled bFGF binding to high-affinity sites was not affected. In view of recent studies demonstrating that the low-affinity receptors of bFGF were heparan sulfate proteoglycans, the authors suggest that the influence of TNP-470 on diminished wound healing is due to its direct recognition by these mols. (c) 2000 Academic Press.

REFERENCE COUNT: 28

REFERENCE(S):
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(3) Broadley, K; Lab Invest 1989, V61, P571 CAPLUS
(5) Galzie, Z; Biochem Cell Biol 1997, V75, P669 CAPLUS
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Searched by Barb O'Bryen STIC 308-4291

(8) Griffith, E; Chem Biol 1997, V4, P461 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 33 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:736476 CAPLUS
DOCUMENT NUMBER: 131:346535
TITLE: Use of neomycin for treating angiogenesis-related diseases
INVENTOR(S): Hu, Guo-Fu; Vallee, Bert L.
PATENT ASSIGNEE(S): The Endowment for Research In Human Biology, Inc., USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958126	A1	19991118	WO 1999-US10269	19990511
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9939804	A1	19991129	AU 1999-39804	19990511
EP 1083896	A1	20010321	EP 1999-922915	19990511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-84921 P 19980511
WO 1999-US10269 W 19990511

AB The present invention is directed to using neomycin or an analog thereof as a therapeutic agent to treat angiogenesis-related diseases, which are characterized by excessive, undesired or inappropriate angiogenesis or proliferation of endothelial cells. The present invention is also directed to pharmaceutical compns. comprising: (a) neomycin or an analog and, optionally, (b) another anti-**angiogenic agent** or an anti-neoplastic agent. The present invention is further directed to a method for screening neomycin analogs having anti-angiogenic activity. A preferred embodiment of the invention relates to using neomycin to treat subjects having such diseases. A dose of 20 ng neomycin/embryo or higher completely inhibited angiogenin-induced angiogenesis in the chorioallantoic membrane (CAM) assay. Neomycin inhibits angiogenin-induced angiogenesis mainly through inhibition of nuclear translocation of angiogenin.

IT **106096-93-9, Basic fibroblast** growth factor
127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neomycin and analogs are inhibitors of nuclear translocation of angiogenic factors for treatment of angiogenesis-related diseases)

REFERENCE COUNT: 1
REFERENCE(S): (1) Waksman; US 2799620 A 1957 CAPLUS

L141 ANSWER 34 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:511254 CAPLUS
DOCUMENT NUMBER: 131:139957
TITLE: New variants of the angiogenic factor vascular endothelial cell growth factor prepared by splicing of

exons with possible therapeutic uses
INVENTOR(S): Baird, Andrew; Andreason, Grai
PATENT ASSIGNEE(S): Collateral Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940197	A2	19990812	WO 1999-US2425	19990204
WO 9940197	A3	19991007		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9925833	A1	19990823	AU 1999-25833	19990204
EP 1053326	A2	20001122	EP 1999-905737	19990204

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:
US 1998-73979 P 19980206
WO 1999-US2425 W 19990204

AB Novel forms of vascular endothelial growth factor encoded by genes with novel arrangements of exons not found amongst natural splicing variants are described. More particularly, novel forms of human **VEGF**-A coded for by genes that contain exon 6b and do not contain exon 6a are disclosed. Other novel forms of the human **VEGF**-A gene contain exon 6b in addn. to exon 6a. These novel forms of **VEGF**-A include **VEGF**-A138, **VEGF**-A162, and **VEGF**-A182. Such novel **VEGF** proteins may be used in treatment of the cardiovascular system and its diseases through effects on anatomy, conduit function, and permeability, and more particularly in the treatment of cardiovascular disease by stimulating vascular cell proliferation using a growth factor, thereby stimulating endothelial cell growth and vascular permeability. The invention also relates to nucleic acids encoding such novel **VEGF** proteins, cells, tissues and animals contg. such nucleic acids; methods of treatment using such nucleic acids; and methods relating to all of the foregoing.

IT **127464-60-2**, **Vascular endothelial growth factor** A
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(new variants of angiogenic factor **VEGF** prepd. by splicing of exons with possible therapeutic uses)

IT **106096-93-9**, Fibroblast growth factor 2
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(potentiation of **VEGF** variant action using; new variants of angiogenic factor **VEGF** prepd. by splicing of exons with possible therapeutic uses)

L141 ANSWER 35 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:325800 CAPLUS
DOCUMENT NUMBER: 130:357131
TITLE: Medicine containing thrombocytes for promoting

cicatrization
INVENTOR(S): Braun, Friedrich; Spaengler, Hans-Peter; Eibl, Johann
PATENT ASSIGNEE(S): Bio-Products & Bio-Engineering Aktiengesellschaft, Austria
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924044	A1	19990520	WO 1998-AT278	19981112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9911354	A1	19990531	AU 1999-11354	19981112
EP 966293	A1	19991229	EP 1998-954056	19981112
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE				
JP 2001508807	T2	20010703	JP 1999-524994	19981112

PRIORITY APPLN. INFO.: AT 1997-1916 A 19971112
WO 1998-AT278 W 19981112

AB A pharmaceutical compn. for local administration to promote cicatrization contains thrombocytes or thrombocyte fragments which contain growth factors capable of being discharged. The thrombocytes are freeze-dried or frozen and are subjected to a process for depleting and/or inactivating viruses. Thus, a human platelet conc. was anticoagulated with 3% Na citrate, centrifuged, washed, dild. to 6 .times. 105/.mu.L, subjected to photodynamic virus inactivation with UV radiation (3.5-4.8 mW/cm2) under CO2/N2 (5:95) at 2-6 psi in the presence of 8-methoxypsoralen, and deep-frozen or lyophilized.

REFERENCE COUNT: 4
REFERENCE(S):
(1) Arlozorov ZG; SU 353724 A
(2) Cryopharm Corp; WO 9117655 A 1991 CAPLUS
(3) Theratechnologies Inc; WO 9734614 A 1997
(4) Valeri, C; Blood 1974, V43(1), P131 CAPLUS

L141 ANSWER 36 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:32099 CAPLUS
DOCUMENT NUMBER: 132:277608
TITLE: changes of **vascular endothelial growth factor** and **basic fibroblast** growth factor content during healing stage of maxillofacial wounds in rabbits
AUTHOR(S): Zhang, Cong-ji; Li, Hui-zeng; Zhou, Shu-xia; Yang, Jun
CORPORATE SOURCE: Southwest Hospital, Third Military Med. Univ., Chungking, 400038, Peop. Rep. China
SOURCE: Di-San Junyi Daxue Xuebao (1999), 21(11), 831-833
CODEN: DYXUE8; ISSN: 1000-5404
PUBLISHER: Di-San Junyi Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The contents of vascular endothelial growth factor (**VEGF**) and basic fibroblast growth factor (bFGF) were detd. in the would discharge of maxillofacial soft tissue after blast injury. The rabbit model of maxillofacial soft tissue blast injury was established with the KTY-04 blasting cap. Wound discharge was collected with polyvinyl alc. sponge

and its content of **VEGF** and bFGF was detd. with ELISA. **VEGF** content in would discharge was increased steadily in the first week after injury. The content was significantly higher in the wound discharge than in the normal serum on the 1st day after injury, it was 2.9 .+-. 2.7 ng/mL on the 3rd day and it reached the peak value on the 7th day ($P < 0.01$). BFGF content in wound discharge reached the peak value (565 .+-. 436 pg/mL) in the 6th hour after injury, was decreased rapidly in the first 1 .apprx. 2 days, returned to the normal level in the 3rd to 5th day and was slightly elevated on the 7th day after injury. **VEGF** and bFGF may take part in 2 angiogenic cascades with synergistic action during the healing stage of maxillofacial blast injury.

IT **106096-93-9, Basic fibroblast** growth factor
127464-60-2, Vascular endothelial growth factor
RL: BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(changes of **vascular endothelial growth factor** and **basic fibroblast** growth factor content during healing stage of maxillofacial wounds in rabbits)

L141 ANSWER 37 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:486428 CAPLUS
DOCUMENT NUMBER: 131:252351
TITLE: Association of heparin with basic fibroblast growth factor, epidermal growth factor, and constitutive nitric oxide synthase on healing of gastric ulcer in rats
AUTHOR(S): Li, Y.; Wang, H. Y.; Cho, C. H.
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, The University of Hong Kong, Hong Kong, Peop. Rep. China
SOURCE: J. Pharmacol. Exp. Ther. (1999), 290(2), 789-796
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The healing effect of heparin on gastric ulcer and its underlying mechanisms were studied. The influences of protamine on these effects were also investigated. Gastric ulcer was induced by acetic acid in rats. Heparin (100-1000 U/kg i.v.) was given once daily for 4 or 7 days. Ulcer area was measured; gastric mucosal regeneration, proliferation, and angiogenesis were detd. by histol. or immunohistochem. methods. Gastric mucosal basic fibroblast growth factor (bFGF) level was assessed by an ELISA, and the mucosal epidermal growth factor (EGF) level and nitric oxide synthase (NOS) activity were measured by RIA. The anticoagulant action of heparin was detd. by the duration of bleeding time. The results showed that heparin given for 4 or 7 days significantly accelerated gastric ulcer healing in a dose-dependent manner. The three doses of heparin significantly stimulated mucosal regeneration and proliferation as well as angiogenesis but not the contraction of ulcer base. Similar effects were obsd. in gastric mucosal bFGF and EGF levels and constitutive NOS activity. Protamine not only abolished the anticoagulant action of heparin but also significantly potentiated its effects on ulcer healing, gastric mucosal proliferation, angiogenesis, and constitutive NOS activity. These findings indicate that heparin can accelerate gastric ulcer healing, which is assocd. with mucosal regeneration, proliferation, and angiogenesis. These actions are likely to be stimulated by bFGF, EGF, and constitutive NOS activity in the gastric mucosa. Protamine potentiates the ulcer-healing effect of heparin, which is probably acting through constitutive NOS activation.

REFERENCE COUNT: 40
REFERENCE(S): (3) Basilico, C; Adv Cancer Res 1992, V59, P115 CAPLUS
(4) Black, S; Cardiovasc Res 1995, V29, P629 CAPLUS

(5) Brzozowski, T; J Gastroenterol 1997, V32, P442 CAPLUS
(7) Folkman, J; Adv Exp Med Biol 1992b, V313, P355 CAPLUS
(9) Folkman, J; Biochem Pharmacol 1985, V34, P905 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 38 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:400788 CAPLUS
DOCUMENT NUMBER: 129:160049
TITLE: **Vascular endothelial growth factor** mediates angiogenic activity during the proliferative phase of wound healing
AUTHOR(S): Nissen, Nicholas N.; Polverini, Peter J.; Koch, Alisa E.; Volin, Michael V.; Gamelli, Richard L.; Dipietro, Luisa A.
CORPORATE SOURCE: Department of Surgery, Loyola University Medical Center, Burn and Shock Trauma Institute, Maywood, IL, 60153, USA
SOURCE: Am. J. Pathol. (1998), 152(6), 1445-1452
CODEN: AJPAA4; ISSN: 0002-9440
PUBLISHER: American Society for Investigative Pathology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Angiogenesis is an essential component of normal wound repair, yet the primary mediators of wound angiogenesis have not been well described. The current study characterizes the contribution of vascular endothelial cell growth factor (**VEGF**) to the angiogenic environment of human surgical wounds. Surgical wound fluid samples (n = 70) were collected daily for up to 7 postoperative days (POD) from 14 patients undergoing mastectomy or neck dissection. **VEGF** levels in surgical wound fluid were lowest on POD 0, approximating values of serum, but increased steadily through POD 7. An opposite pattern was noted for basic fibroblast growth factor-2. Fibroblast growth factor-2, which has been previously described as a wound angiogenic factor, exhibited highest levels at POD 0, declining to near serum levels by POD 3. Surgical wound fluid from all time points stimulated marked endothelial cell chemotaxis and induced a brisk neovascular response in the rat corneal micropocket angiogenesis assay. Antibody neutralization of **VEGF** did not affect the in vitro chemotactic or the in vivo angiogenic activity early wound samples (POD 0). In contrast, **VEGF** neutralization significantly attenuated both chemotactic activity (mean decrease 76 .+-. 13%, $P < 0.01$) and angiogenic activity (5 of 5 samples affected) of later wound samples (POD 3 and 6). The results suggest a model of wound angiogenesis in which an initial angiogenic stimulus is supplied by fibroblast growth factor-2, followed by a subsequent and more prolonged angiogenic stimulus mediated by **VEGF**.

IT **127464-60-2, Vascular endothelial growth factor**
RL: **BAC (Biological activity or effector, except adverse)**; BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**vascular endothelial growth factor** mediates angiogenic activity during the proliferative phase of wound healing)

IT **106096-93-9**, Fibroblast growth factor-2
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**vascular endothelial growth factor** mediates angiogenic activity during the proliferative phase of wound healing)

L141 ANSWER 39 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:353617 CAPLUS
DOCUMENT NUMBER: 129:36331
TITLE: Accelerating mechanisms of marzulene-S in ulcer healing. 1. Effects of **angiogenesis** and bFGF activity in chronic gastric ulcer model
AUTHOR(S): Hayashi, Keiichiro
CORPORATE SOURCE: Research Laboratories, Kotobuki Pharmaceutical Co., Ltd., Japan
SOURCE: Yakuri to Chiryo (1998), 26(4), 465-473
CODEN: YACHDS; ISSN: 0386-3603
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The effects of marzulene-S on ulcer healing were compared with sucralfate, ecabet sodium, and ranitidine in rats with exptl. chronic gastric ulcer. The results indicated that marzulene-S accelerates ulcer healing by promoting angiogenesis and inhibiting bFGF degrdn.

L141 ANSWER 40 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:489350 CAPLUS
DOCUMENT NUMBER: 129:243509
TITLE: Coordinated induction of **VEGF** receptors in mesenchymal cell types during rat hepatic wound healing
AUTHOR(S): Ankoma-Sey, V.; Matli, M.; Chang, K. B.; Lalazar, A.; Donner, D. B.; Wong, L.; Warren, R. S.; Friedman, S. L.
CORPORATE SOURCE: UCSF Liver Center Dep. Medicine Surgery, Univ. California, San Francisco, CA, USA
SOURCE: Oncogene (1998), 17(1), 115-121
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Homol. PCR has been used to identify receptor tyrosine kinases (RTKs) expressed during activation of rat hepatic stellate cells, the key fibrogenic mesenchymal element in the liver. Partial cDNAs encoding several RTKs were cloned from stellate cells activated in vivo, including those of Flt-1, Flk-1, c-met, PDGFR, and Tyro 10/DDR2. RNase protection from cells activated in vivo demonstrated biphasic induction of flt-1 and flk-1 mRNAs, receptors for vascular endothelial growth factor (**VEGF**). Culture-activation of stellate cells was assocd. with increased [125I]**VEGF** binding and Flt-1 and Flk-1 receptor protein. Induction of **VEGF** binding sites correlated with an 2.5-fold increase in DNA synthesis in response to **VEGF**, but only if cells were activated by growth on collagen I, whereas cells maintained in a quiescent state on a basement membrane-like substratum (EHS matrix) were nonproliferative. In both stellate and endothelial cells **VEGF**-induced mitogenesis was augmented by co-incubation with basic fibroblast growth factor (bFGF), a cytokine with known synergy with **VEGF**. These findings suggest that the cellular targets of **VEGF** in liver may not be confined to sinusoidal endothelial cells, and that **VEGF** responses reflect combined effects on both hepatic stellate cells and sinusoidal endothelium.
IT **127464-60-2, Vascular endothelial growth factor**
RL: **BAC (Biological activity or effector, except adverse)**; BIOL (Biological study)
(coordinated induction of **VEGF** receptors in mesenchymal cell types during rat hepatic wound healing)
IT **106096-93-9, Basic fibroblast** growth factor

RL: **BAC (Biological activity or effector, except adverse)**; BIOL (Biological study)
(coordinated induction of **VEGF** receptors in mesenchymal cell types during rat hepatic wound healing in relation to)

L141 ANSWER 41 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:506326 CAPLUS
DOCUMENT NUMBER: 127:117385
TITLE: Anti-idiotypic antibodies to vascular endothelial growth factor for control of **angiogenesis**
INVENTOR(S): Plouet, Jean; Jonca, Frederic; Ortega, Nathalie; Ruchoux, Marie-magdeleine
PATENT ASSIGNEE(S): Centre National De La Recherche Scientifique, Fr.; Plouet, Jean; Jonca, Frederic; Ortega, Nathalie; Ruchoux, Marie-Magdeleine
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723510	A1	19970703	WO 1996-FR2041	19961220
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2742662	A1	19970627	FR 1995-15243	19951221
FR 2742662	B1	19980123		
EP 868434	A1	19981007	EP 1996-943157	19961220
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 2000506501	T2	20000530	JP 1997-523366	19961220

PRIORITY APPLN. INFO.: FR 1995-15243 19951221
WO 1996-FR2041 19961220

AB Anti-idiotypic antibodies to vascular endothelial growth factor (VEGF) are used to control VEGF activity to control angiogenesis, either inhibiting or promoting angiogenesis without affecting quiescent endothelial cells. or for prepg. a product for th diagnosis of diseases involving endothelial cells undergoing an angiogenesis process. The antibodies can also be used in the diagnosis of diseases involving endothelial angiogenesis. The antibodies are used as ligands for the KDR receptor.

L141 ANSWER 42 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:561889 CAPLUS
DOCUMENT NUMBER: 127:232974
TITLE: Conjunctival fibrosis in ocular cicatricial pemphigoid-the role of cytokines
AUTHOR(S): Elder, Mark J.; Dart, John K. G.; Lightman, Susan
CORPORATE SOURCE: Institute of Ophthalmology, Moorfields Eye Hospital, Christchurch, N. Z.
SOURCE: Exp. Eye Res. (1997), 65(2), 165-176
CODEN: EXERA6; ISSN: 0014-4835
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ocular cicatricial pemphigoid (OCP) is a systemic, autoimmune disease characterized by conjunctival scarring that is often progressive. The pathophysiol. of the fibrosis is unknown. This study aimed to det. which fibrogenic cytokines are present in the conjunctiva in patients with acute and chronic OCP as a first stage in detg. the mechanisms of fibrosis. Conjunctival biopsies from patients with acute, subacute and chronic OCP (n = 13) were compared to normal conjunctiva (n = 10). Prodn. of mRNA for, and expression of, transforming growth-.beta.1, 2 and 3 (TGF-.beta.),

TGF-.beta. receptor, platelet derived growth factor (PDGF) and fibroblast growth factor (FGF) were assessed using in situ hybridization and immunohistochem. Acute disease showed increased levels of mRNA for TGF-.beta.1 and 3, mainly in stromal fibroblasts and macrophages. In the stroma, there were concordant increases in latent and activated TGF-.beta.1 and 3 and TGF-.beta. receptor expression by fibroblasts. There were no significant increases in the expression of TGF-.beta.2, PDGF or FGF in acute disease. No cytokines or receptors were significantly increased in chronic disease. Acutely inflamed conjunctiva in OCP is assocd. with significant stromal levels of TGF-.beta.1 and 3 but not PDGF or FGF and none were increased in chronic disease. This suggests that TGF-.beta. may have a key role in the pathogenesis of the fibrosis. The absence of fibrogenic cytokines in chronic progressive OCP provides support for the proposal that fibroblasts in OCP conjunctiva may remain functionally and morphol. abnormal after the withdrawal of cytokine influences.

L141 ANSWER 43 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:987768 CAPLUS
DOCUMENT NUMBER: 124:75905
TITLE: Suppression of collagen-induced arthritis by an **angiogenesis** inhibitor, AGM-1470, in combination with cyclosporin: reduction of vascular endothelial growth factor (VEGF)
AUTHOR(S): Oliver, Stephen J.; Cheng, Tammy P.; Banquerigo, Mona Lisa; Brahn, Ernest
CORPORATE SOURCE: Division of Rheumatology, UCLA School of Medicine, Los Angeles, CA, 90095, USA
SOURCE: Cell. Immunol. (1995), 166(2), 196-206
CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pannus formation characterized by neovascularization is a prominent pathol. finding in both rheumatoid arthritis (RA) and rat collagen-induced arthritis (CIA). CIA is a T-cell dependent process induced by immunization of inbred LOU rats with native type II collagen in incomplete Freund's adjuvant. AGM-1470 is a highly specific inhibitor of new blood vessel formation by its effects on endothelial cell migration, endothelial cell proliferation, and capillary tube formation. Cyclosporin A (CSA) is a immunomodulating agent that inhibits IL-2 and other cytokine prodn. involved in early antigen activation of T-cells. In this study the effects of single and combination therapy with AGM-1470 (27 mg/kg alternate days) and low-dose CSA (4 mg/kg/day continuous infusion via osmotic pump) on established CIA (total) were examd. At Day 18 post arthritis onset, clin. arthritis was significantly reduced in rats treated with single-agent AGM-1470 (1.88) or combination therapy (1.13) (and 0.000001, resp.) vs. control. Single-agent CSA-treated rats, even if given CSA beginning on the day of immunization, did not attenuate arthritis severity. The longitudinal mean arthritis score of combination-treated rats was significantly lower than that of rats receiving AGM-1470, reflecting a more moderate early disease course in combination-treated rats. Disease severity in rats treated with single-agent CSA was not significantly different from control rats. Mean WBC counts, differentials, and delayed-type hypersensitivity responses were similar in all groups. CII antibody levels were lower in AGM-1470 protocols compared to CSA or controls. Flow cytometry of peripheral blood, spleen, and lymph nodes demonstrated decreased levels of CD4+ cells in rats given CSA. TNF-.alpha. levels remained elevated, even in treated rats, while vascular endothelial growth factor levels were reduced in rats receiving AGM-1470 compared to both arthritic controls and naive rats. Both single-agent and combination therapies were well tolerated. This is the first study to examine the effects of AGM-1470 together with CSA. Combination therapy was more effective than single-agent therapy. The

results suggest that the use of interventions with distinct mechanisms of action may be efficacious in the treatment of RA.

L141 ANSWER 44 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:620063 CAPLUS
DOCUMENT NUMBER: 117:220063
TITLE: Cicatrizant from blood plasma supernatant
INVENTOR(S): Lawny, Francois
PATENT ASSIGNEE(S): Fondation Nationale de Transfusion Sanguine, Fr.
SOURCE: Fr. Demande, 11 pp.
CODEN: FRXXBL

DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2667789	A1	19920417	FR 1990-12742	19901016

AB A cicatrizant is obtained by activating the transforming growth factor-.beta. in the supernatant of human or animal blood platelets. Activation is carried out by exposure to pH <5. Blood platelets are treated with thrombin, followed by centrifuging. The supernatant, adjusted to pH 7, is heated at 60.degree. for 10 min, followed by adjustment to pH 2.5 (HCl). After 10 min, NaOH is added to pH 7 and the ppt. is centrifuged off. The supernatant is a cicatrizant, as shown in rats.

L141 ANSWER 45 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:548031 CAPLUS
DOCUMENT NUMBER: 111:148031
TITLE: Synthetic genes encoding growth factors, and manufacture of the factors for use as **angiogenic agents** and in cell culture
INVENTOR(S): Gruss, Peter; Knoerzer, Wiebke; Schnoelzer-Rackwitz, Martina; Rackwitz, Hans Richard
PATENT ASSIGNEE(S): Progen Biotechnik G.m.b.H., Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 297262	A2	19890104	EP 1988-107849	19880517
EP 297262	A3	19890201		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
DE 3721081	A1	19890119	DE 1987-3721081	19870626
JP 01291797	A2	19891124	JP 1988-156595	19880624
PRIORITY APPLN. INFO.:			DE 1987-3721081	19870626
			EP 1988-107849	19880517

AB Synthetic genes for acidic and basic fibroblast growth factors (a- and bFGFs, resp.) are prepd. and expressed in Escherichia coli. The recombinant FGFs can be used as a component of cell culture media and for angiogenesis, e.g. for wound healing. A synthetic gene for human bFGF type 1 with codons optimized for expression in E. coli was constructed. This gene was inserted into pUC12. E. coli transformed with this plasmid produced FGF which was isolated and purified. Similar FGFs were tested in cell culture medium and for stimulation of capillary growth and wound healing.

IT **106096-93-9, Basic fibroblast** growth factor
RL: PRP (Properties)
(synthetic gene for, expression in Escherichia coli of)

L141 ANSWER 46 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001222505 EMBASE
TITLE: Expression of decorin and biglycan in rat gastric tissue: Effects of ulceration and basic fibroblast growth factor.
AUTHOR: Pohle T.; Altenburger M.; Shahin M.; Konturek J.W.; Krèsse H.; Domschke W.
CORPORATE SOURCE: Dr. T. Pohle, Dept. of Medicine B, University of Munster, D-48129 Munster, Germany. pohlet@uni-muenster.de
SOURCE: Scandinavian Journal of Gastroenterology, (2001) 36/7 (683-689).
Refs: 38
ISSN: 0036-5521 CODEN: SJGRA4
COUNTRY: Norway
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: The small chondroitin/dermatan sulphate proteoglycans decorin and biglycan participate in organizing the network of collagen fibrils and interact with non-collagenous matrix proteins. In addition, via interactions with cytokines they are directly or indirectly involved in signalling, growth and cell differentiation. We aimed to analyse their expression in normal gastric tissue and during gastric ulcer healing. Methods: Proteoglycan expression was studied by immunohistochemistry and in situ hybridization in acetic acid-induced gastric ulcers in rat during early phases and during chronic ulceration. The effects of treatment with an acid stable mutein of FGF-2 (bFGF) were also studied. Results: In normal gastric tissue, both proteoglycans were most strongly expressed in the submucosal layer. However, some epithelial cells were positive for biglycan and, surprisingly, also for decorin. In the early phase after ulcer induction exclusively decorin became induced in the muscularis mucosae, while biglycan became detectable in this layer only after 2 weeks. There was no up-regulation of either proteoglycan in other layers, nor could an effect of FGF-2 treatment be seen. Conclusions: The expression of decorin could be observed for the first time in epithelial cells. Decorin, but not biglycan, appears as an early phase reactant in the muscularis mucosae in accordance with its putative role during angiogenesis and the prevention of apoptosis.

L141 ANSWER 47 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001090712 EMBASE
TITLE: Impaired angiogenesis in the aging kidney: Vascular endothelial growth factor and thrombospondin-1 in renal disease.
AUTHOR: Kang D.-H.; Anderson S.; Kim Y.-G.; Mazzalli M.; Suga S.-I.; Jefferson J.A.; Gordon K.L.; Oyama T.T.; Hughes J.; Hugo C.; Kerjaschki D.; Schreiner G.F.; Johnson R.J.
CORPORATE SOURCE: Dr. D.-H. Kang, Division of Nephrology, Baylor College of Medicine, Alkek N730, One Baylor Plaza, Houston, TX 77030, United States. dkang@bcm.tmc.edu
SOURCE: American Journal of Kidney Diseases, (2001) 37/3 (601-611).
Refs: 48
ISSN: 0272-6386 CODEN: AJKDDP
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy

020 Gerontology and Geriatrics
028 Urology and Nephrology
029 Clinical Biochemistry

LANGUAGE: English
SUMMARY LANGUAGE: English

AB We investigated the relationship of changes in the microvasculature to age-related structural and functional changes in the kidney to determine whether there was evidence of impaired angiogenesis and whether the loss of microvasculature could be accounted for by changes in the local production of angiogenic or antiangiogenic factors. Glomerular and peritubular capillary number, density, and endothelial cell proliferation were determined in aging (24 months; n = 9) and young (3 months; n = 8) rat kidneys and correlated with renal functional and structural changes and alterations in renal expression of vascular endothelial growth factor (VEGF) and thrombospondin-1 (TSP-1). Aging rats showed a focal decrease in both peritubular capillary (peritubular capillary staining, 5.4% .+-. 1.8% versus 11.3% .+-. 2.0% per 100 tubules; rarefaction index, 10.6% .+-. 4.6% versus 0.6% .+-. 0.1%, aging versus young rats; P < 0.05 and P < 0.001, respectively) and glomerular capillary loops (27.3 .+-. 6.9 versus 50.7 .+-. 7.4/glomerulus, aging versus young rats; P < 0.001). The number of proliferating endothelial cells was decreased in aging rats compared with young rats (glomerular, 0.04 .+-. 0.01 versus 0.15 .+-. 0.03 positive cells/glomerular cross-section; peritubular, 0.7 .+-. 0.2 versus 4.3 .+-. 2.6 positive cells/mm(2); P < 0.05). In the aging kidney, VEGF expression was focally increased in the cortex compared with young rats, whereas a profound decrease was observed in the outer and inner medulla (total area of VEGF expression, 19.2% .+-. 11.4% versus 39.3% .+-. 7.6%; P < 0.05). Tubular VEGF expression correlated with peritubular capillary density (r(2) = 0.57; P < 0.01) and inversely correlated with tubular osteopontin (r(2) = -0.55; P < 0.05) and macrophage infiltration (r(2) = -0.64; P < 0.01). TSP-1 staining was increased in the glomeruli and tubulointerstitium of the aging rats. Glomerular TSP-1 score correlated inversely with glomerular capillary number (r(2) = -0.89; P < 0.001). Tubulointerstitial TSP-1 also correlated with percentage of positive staining of peritubular capillary (r(2) = -0.59; P < 0.001). Glomerular capillary number showed significant correlation with glomerulosclerosis score, as well as with 24-hour urinary protein excretion. Peritubular capillary density also inversely correlated with interstitial fibrosis score and urinary protein excretion. In conclusion, glomerular and peritubular capillary loss in the aging kidney correlate with alterations in VEGF and TSP-1 expression and also with the development of glomerulosclerosis and tubulointerstitial fibrosis. These findings suggest that impaired angiogenesis associated with progressive loss in renal microvasculature may have a pivotal role in age-related nephropathy.

L141 ANSWER 48 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001274273 EMBASE
TITLE: Are basic fibroblast growth factor and vascular endothelial growth factor prognostic indicators in pediatric patients with malignant solid tumors?.
AUTHOR: Tabone M.-D.; Landman-Parker J.; Arcil B.; Coudert M.-C.; Gerota I.; Benbunan M.; Leverger G.; Dosquet C.
CORPORATE SOURCE: M.-D. Tabone, Serv. d'Hematol./d'Oncol. Pediatr., Hopital d'Enfant Armand Trousseau, 26 avenue du Docteur Arnold Netter, 75012 Paris, France. marido_tabone@yahoo.fr
SOURCE: Clinical Cancer Research, (2001) 7/3 (538-543).
Refs: 42
ISSN: 1078-0432 CODEN: CCREF4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
016 Cancer

029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Angiogenesis plays an important role in the growth, progression, and metastasis of solid tumors. Among angiogenic factors, basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF) appear to be useful markers in adults with cancer. The aim of this pilot study was to determine the levels of VEGF in serum and bFGF in serum and urine of children with solid tumor at diagnosis (as measured by ELISA), and to investigate whether these parameters provide prognostic information. Forty consecutive patients with different types of cancer were prospectively included in this study. Median values of all studied angiogenic factors were higher in patients than in controls (n = 40), and the differences were statistically significant for bFGF in serum and urine: 10 versus 3 pg/ml (P = 0.0004) and 6406 versus 0 pg/g of creatinine (P < 0.0001), respectively. Among patients, median serum values of bFGF and VEGF were higher in children with metastatic disease (n = 14) than in those with localized disease (n = 26). The difference was statistically significant for serum bFGF: 17.5 versus 6 pg/ml (P = 0.02). Serum angiogenic factor levels correlated with outcome. The estimated event-free survival at 3 years was 79% for patients with normal bFGF values (n = 13) versus 42% (n = 26; P = 0.02) for those with high levels, and 71% in case of normal VEGF values (n = 20) versus 38% (n = 19; P = 0.04) for those with high levels. No benefit of normal urinary bFGF values was observed. Our results provide a rationale for exploring the clinical interest of bFGF and VEGF measurements in body fluids of a larger group of children with cancer.

L141 ANSWER 49 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001356990 EMBASE
TITLE: Effect of local injection with basic fibroblast growth factor (BFGF) and neutralizing antibody to BFGF on gastric ulcer healing, gastric secretion, angiogenesis and gastric blood flow.
AUTHOR: Ernst H.; Konturek P.C.; Hahn E.G.; Stosiek H.P.; Brzozowski T.; Konturek S.J.
CORPORATE SOURCE: Dr. H. Ernst, Department of Gastroenterology, Carl-Thiem-Klinikum, Postfach 100 363, 03003 Cottbus, Germany. 4.Med.Klinik@ctk.de
SOURCE: Journal of Physiology and Pharmacology, (2001) 52/3 (377-390).
Refs: 22
ISSN: 0867-5910 CODEN: JPHPEI
COUNTRY: Poland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Exogenous administration of bFGF was shown to accelerate tissue repair predominantly due to an increase in the formation of new microvessels (angiogenesis) suggesting that bFGF plays an important role in healing of gastric ulcer. This study was designed: 1) to examine the effect of local application of bFGF with or without neutralizing antibody (NA) to bFGF and 2) to determine the role of gastric secretion, gastric blood flow (GBF) at the ulcer margin and angiogenesis during gastric ulcer healing with or without local application of NA, bFGF or the combination of NA and bFGF. Chronic gastric ulcers were induced in Wistar rats by subserosal application of acetic acid (ulcer area 28 mm(2)) and gastric secretion during ulcer healing was assessed using animals additionally equipped with chronic gastric fistulas. The bFGF without or with NA to bFGF (10 ng/100 .mu.l), irrelevant antibodies (rabbit IgG; 10 .mu.g/100 .mu.l) or vehicle (saline) were locally injected into the subserosa immediately upon ulcer

induction (day 0) and at day 2. Rats with acetic acid ulcers without subserosal injections served as controls. At day 11, all animals were anaesthetized and GBF was determined at the ulcer base, ulcer margin as well as in intact mucosa using the H(2)-gas clearance technique and the area of gastric ulcers was measured by planimetry. Gastric mucosa with ulcer was excised and the percentage of area covered with blood vessels, the number of fibroblasts and the percentage of connective tissue at the ulcer edge was assessed by histology. The gastric ulcers were healed spontaneously in control vehicle-treated rats at day 11 and this was accompanied by the significant increase in the GBF and number of microvessels in the ulcer area. The gastric secretion was suppressed immediately after ulcer induction and increased significantly at day 2 and day 11 but failed to return to that recorded in intact animals. In contrast, local application of bFGF inhibited gastric acid and pepsin outputs at each study time intervals tested and this effect was reversed by addition of NA to bFGF. Locally applied bFGF accelerated significantly ulcer healing and this was accompanied by the greater rise in the GBF of ulcer margin and more marked increase in number of microvessels as compared to those in vehicle-treated rats. Subserosal application of NA to bFGF prolonged significantly the ulcer healing and this effect was accompanied by a significant fall in the GBF at the ulcer margin and a decrease in number of capillaries in ulcer bed without significant alteration in gastric acid and pepsin outputs. The ulcer healing effect of bFGF and accompanying increase in the GBF at ulcer margin and in the number of microvessels as well as inhibition of gastric acid secretion evoked by bFGF were significantly attenuated by the addition of NA to bFGF. The number of fibroblasts and the distribution of connective tissue did not differ between groups studied. We conclude that; 1) depletion of endogenous bFGF at the ulcer area by specific NA to bFGF delays healing of gastric ulcers, reduces angiogenesis of ulcer bed and impairs the microcirculatory effect of this growth factor at the ulcer margin indicating that the availability of bFGF in the ulcer area plays a crucial role in the ulcer healing through induction of angiogenesis; 2) this prominent antiulcer effect of locally applied bFGF depends, at least in part, upon the inhibition of acid secretion by this peptide.

L141 ANSWER 50 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001384700 EMBASE
TITLE: Gene expression and gene therapy in experimental duodenal ulceration.
AUTHOR: Szabo S.; Deng X.; Khomenko T.; Yoshida M.; Jadus M.R.; Sandor Z.; Gombos Z.; Matsumoto H.
CORPORATE SOURCE: S. Szabo, Lab. Med. Service, VA Medical Center, 5901 E. 7th Street, Long Beach, CA 90822-5201, United States. sandor.szabo@med.va.gov
SOURCE: Journal of Physiology Paris, (2001) 95/1-6 (325-335). Refs: 85
ISSN: 0928-4257 CODEN: JHYSEM
PUBLISHER IDENT.: S 0928-4257(01)00045-6
COUNTRY: France
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Gastroduodenal ulceration is still poorly understood and changes in gene expression may provide new mechanistic insights. Previously, we demonstrated that angiogenic growth factors are potent ulcer healing agents, and the synthesis of bFGF, PDGF and VEGF is enhanced early in duodenal ulcer healing. The initial molecular event in duodenal ulceration seems to be the organ-specific early release of ET-1 in the

pre-ulcerogenic stages after the administration of duodenal ulcerogen cysteamine in rats. We also briefly review here data from literature indicating a central role of ET-1 in gastroduodenal ulceration. After studying the involvement of immediate early genes (e.g, egr-1, Sp1) in ulcer development, we now investigated expression of other genes in the duodenal mucosa in the early stages of chemically induced duodenal ulceration in rats. Following a brief review of principles of gene expression and gene therapy, we review our preliminary gene expression studies, involving monitoring about 1200 genes which revealed about 160 signals and prominent changes in about 30 genes in the early stages of experimental duodenal ulceration. Cysteamine enhanced ET-B receptor gene expression in 30 min, while transcription factors (MAX, STAT 3) showed increased expression in 12 h. We recently also initiated gene therapy studies to enhance the local synthesis of PDGF and VEGF to accelerate duodenal ulcer healing, using a single dose of naked DNA (ND) or adenoviral (AV) vectors of VEGF and PDGF in rats with cysteamine-induced duodenal ulcers. Gene therapy with ND or AV of VEGF or PDGF significantly accelerated chronic duodenal ulcer healing, and increased levels of VEGF and PDGF were detected by Western blotting and ELISA in duodenal mucosa after both VEGF and PDGF gene therapy. Thus, gene expression studies provide new insights into the molecular mechanisms of duodenal ulceration and VEGF or PDGF gene therapy seems to be a new option to achieve a rapid ulcer healing. .COPYRGT. 2001 Published by Elsevier Science Ltd.

L141 ANSWER 51 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000248397 EMBASE
TITLE: Cytoplasmic dynein conversion at a crush injury in rat peripheral axons.
AUTHOR: Li J.-Y.; Pfister K.K.; Brady S.T.; Dahlstrom A.
CORPORATE SOURCE: Dr. J.-Y. Li, Dept. of Anatomy and Cell Biology, University of Goteborg, Box 420, SE 405 30 Goteborg, Sweden. jiayi.li@anatcell.gu.se
SOURCE: Journal of Neuroscience Research, (15 Jul 2000) 61/2 (151-161).
Refs: 53
ISSN: 0360-4012 CODEN: JNREDK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cytoplasmic dynein is a motor for retrograde axonal transport for movement of membranous organelles toward the neuronal cell body. However, cytoplasmic dynein is synthesized in the cell body and conveyed along the axon to nerve terminals. To characterize the axonal transport of cytoplasmic dynein in relation to synaptic vesicles and other membrane compartments, immunocytochemical and cytofluorimetric scanning analyses of crush-operated rat sciatic nerves were performed. Distal to the crush, the kinetics of dynein accumulation were consistent with its role in the retrograde transport of membranous organelles. During the initial 3 hr after crush, only small amounts of dynein-immunoreactive material accumulated proximal to the crush. This is consistent with metabolic labeling studies showing that most of the dynein moving in the anterograde direction is in the slow component of axonal transport. Thereafter, the rate of proximal accumulation of dynein increased, and by 8 hr postcrush a large amount of dynein immunoreactivity was observed. This accelerated accumulation may be due to recruitment of dynein from slow **component b** onto organelles proximal to the crush.
Double labeling demonstrated that dynein immunoreactivity colocalized with synaptophysin, a transmembrane protein found in small, clear synaptic vesicles. In contrast, dynein immunoreactivity did not colocalize well with calcitonin generelated peptide (CGRP), a peptide matrix marker for some large dense-cored vesicles. Finally, dynein immunoreactivity

colocalized with the anterograde transport motor kinesin both proximal and distal to a crush, suggesting that kinesin may carry some dynein-containing membrane compartments during fast anterograde axonal transport. (C) 2000 Wiley-Liss, Inc.

L141 ANSWER 52 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999359725 EMBASE
TITLE: Axonal transport of synucleins is mediated by all rate components.
AUTHOR: Jensen P.H.; Li J.-Y.; Dahlstrom A.; Dotti C.G.
CORPORATE SOURCE: Dr. P.H. Jensen, Department of Medical Biochemistry, University of Aarhus, Ole Worms Alle, Bygn. 170, DK-8000 Aarhus C, Denmark. phj@biokemi.au.dk
SOURCE: European Journal of Neuroscience, (1999) 11/10 (3369-3376). Refs: 44
ISSN: 0953-816X CODEN: EJONEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
002 Physiology
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Synucleins are abundant nerve terminal proteins of hitherto unknown function. In diseases with Lewy bodies, human .alpha.-synuclein concentrates in these lesions in the cell body and mutations in .alpha.-synuclein lead to heritable Parkinson's disease with Lewy bodies. This indicates that changes in the normal metabolism and axonal transport of .alpha.-synuclein is perturbed in these diseases. To investigate the normal axonal transport of synucleins we studied the rat visual system by nerve crush operations and metabolic labelling of the retinal ganglion cells followed by immunoprecipitation of nerve segments. We found by immunofluorescence microscopy of the crush-operated nerves that synucleins are transported by fast antero- and retrograde transport and colocalize with synaptophysin and SNAP-25 around the lesion. The metabolic labelling studies demonstrated that synucleins were moved through the nerve with all the rate components, the fast component and the slow components a and b, with **component b** predominating. Two-dimensional gel electrophoresis revealed that both .alpha.- and .beta.-synuclein migrate through the nerve by slow **component b** in a ratio of 2:1.

L141 ANSWER 53 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999382996 EMBASE
TITLE: Effect of basic fibroblast growth factor on gastric ulcer healing and its own mRNA expression.
AUTHOR: Pohle T.; Shahin M.; Domschke W.; Konturek J.W.
CORPORATE SOURCE: Dr. T. Pohle, Department of Medicine B, University of Munster, Albert-Schweitzer-Str. 33, D-48129 Munster, Germany. pohlet@uni-muenster.de
SOURCE: Alimentary Pharmacology and Therapeutics, (1999) 13/11 (1543-1551). Refs: 27
ISSN: 0269-2813 CODEN: APTHEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: The application of an acid-stable mutein of basic fibroblast growth factor (bFGF) called CS23 results in acceleration of ulcer healing. The modes by which this cytokine exerts these effects are not yet

completely understood. Aim: To describe the pattern of bFGF-mRNA expression during ulcer healing and to examine the effects of exogenously applied CS23 on gastric ulcer healing in an animal model. Methods: The speed of healing of gastric ulcers, expression of extracellular matrix gene mRNAs such as pro .alpha.(I) collagen (by non-radioactive in situ hybridization), cellular proliferation evidenced by the display of PCNA (by immunohistochemistry), angiogenesis, and the feedback of this growth factor on its own mRNA expression pattern were used to evaluate the effects of CS23 on rat gastric ulcer healing in an animal model. Results: CS23 accelerates gastric ulcer healing at 7, 14 and 21 days after ulcer induction. We found an increase in connective tissue beneath the ulcer bed in treated animals in comparison to controls. The expression of PCNA as well as pro .alpha.(I) collagen mRNA was markedly increased in ulcers, yet there was no distinct difference between treatment arms. In contrast, the density of microvessels was significantIy increased in the submucosa of ulcers by CS23 application. bFGF-mRNA expression is up-regulated in the submucosa during early ulcer healing; this increase diminishes within days but can be restituted by the exogenous application of CS23. Conclusions: CS23 speeds gastric ulcer healing and significantly increases the density of microvessels in the ulcerated tissue. Without affecting the numbers of proliferating cells or the transcription of collagen mRNA. In addition, it augments the expression of bFGF-mRNA during the later stages of healing, suggesting a positive feedback loop.

L141 ANSWER 54 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999196061 EMBASE
TITLE: Antiangiogenic therapy of a recurrent giant cell tumor of the mandible with interferon alfa-2a.
AUTHOR: Kaban L.B.; Mulliken J.B.; Ezekowitz R.A.; Ebb D.; Smith P.S.; Folkman J.
CORPORATE SOURCE: Dr. L.B. Kaban, Dept. of Oral/Maxillofacial Surg., Massachusetts General Hospital, Boston, MA 02114, United States
SOURCE: Pediatrics, (1999) 103/6 I (1145-1149).
Refs: 48
ISSN: 0031-4005 CODEN: PEDIAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
011 Otorhinolaryngology
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We report a 5-year-old girl with a large rapidly growing giant cell tumor of the mandible that recurred 2 months after the first surgical excision and 3 months after a second resection. An angiogenic protein, (bFGF), was abnormally elevated in her urine. The patient was treated with interferon alfa-2a for 1 year because this agent inhibits angiogenesis by suppressing bFGF overexpression in infantile hemangiomas and in other human tumors. During this time the bone tumor regressed and disappeared, the urinary bFGF fell to normal levels, and the mandible regenerated. She has remained tumor-free and has been off therapy for 3 years at this writing. This first successful use of interferon alfa-2a to treat a mandibular tumor in a child demonstrates: 1) low grade tumors that overexpress bFGF may respond to interferon alfa-2a, in a manner similar to life-threatening infantile hemangiomas; 2) antiangiogenic therapy, given without interruption for 1 year, was safe and effective in this patient; and 3) treatment may be continued for 1 year without the development of drug resistance.

L141 ANSWER 55 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97359944 EMBASE

DOCUMENT NUMBER: 1997359944
TITLE: Angiogenesis in the pathobiology and treatment of vascular and malignant diseases.
AUTHOR: Winlaw D.S.
CORPORATE SOURCE: Dr. D.S. Winlaw, Department of Cardiothoracic Surgery, St Vincent's Hospital, Victoria St, Darlinghurst, NSW 2010, Australia. dwinlaw@wr.com.au
SOURCE: Annals of Thoracic Surgery, (1997) 64/4 (1204-1211).
Refs: 79
ISSN: 0003-4975 CODEN: ATHSAK
PUBLISHER IDENT.: S 0003-4975(97)00716-9
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cardiovascular disease and cancer account for the majority of adult disease in the developed world. This review focuses on current concepts in the study of angiogenesis (new vessel formation) as related to these conditions and highlights the role of vascular endothelial growth factor. Developments in therapeutic angiogenesis have raised the possibility that pharmacologic or gene-directed interventions, based on the ability of vascular endothelial growth factor to promote new vessel formation, may soon gain clinical application for the treatment of occlusive vascular disease. Similarly, the future treatment of malignant disease is likely to involve antiangiogenic agents that, in preliminary animal work, have demonstrated an efficacy that is not limited by adverse affects. Aside from these potential applications, current investigations have enhanced our understanding of mechanisms involved in the development of atherosclerotic and malignant disease.

L141 ANSWER 56 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97118561 EMBASE
DOCUMENT NUMBER: 1997118561
TITLE: Manipulating angiogenesis: From basic science to the bedside.
AUTHOR: Pepper M.S.
CORPORATE SOURCE: Dr. M.S. Pepper, Departement de Morphologie, Centre Medical Universitaire, 1 rue Michel-Servet, 1211 Geneve 4, Switzerland
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology, (1997) 17/4 (605-619).
Refs: 166
ISSN: 1079-5642 CODEN: ATVBFA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Considerable progress has been made recently in understanding the molecular mechanisms of angiogenesis, which like most other biological processes is the result of subtle and often complex interactions between molecules that have regulatory (eg, cytokines and their receptors) and effector (eg, extracellular matrix, integrins, and proteases) functions. The title of this review was chosen to reflect a recent trend in which knowledge acquired through a molecular/cell biological approach is being rapidly transferred to the clinical setting. As a result, by manipulating

angiogenesis either positively or negatively, considerable therapeutic benefit can now be envisaged in physiological and pathological settings in which neovascularization is a prominent component.

L141 ANSWER 57 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97343820 EMBASE
DOCUMENT NUMBER: 1997343820
TITLE: Recombinant bFGF promotes wound healing after ballistic injury.
AUTHOR: Zheng J.-X.; Wang S.-H.; Guo L.-L.; Yan D.-A.
CORPORATE SOURCE: Dr. J.-X. Zheng, Department of Hematology, Zhu Jing Hospital, First Military Medical College, Guangzhou 510282, China
SOURCE: Asian Journal of Surgery, (1997) 20/4 (320-323).
Refs: 7
ISSN: 1015-9584 CODEN: AJSUEF
COUNTRY: Hong Kong
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
049 Forensic Science Abstracts
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The effects of basic fibroblast growth factor (bFGF) on promoting wound healing were studied in an attempt to discover new methods of treating ballistic injury. The effects of recombinant bFGF and factors influencing these effects in rabbits with ballistic injury were studied. The right hind legs of rabbits were shot with a pistol, after which bFGF was used to treat the wound tracks. The time required for ballistic wound track healing was shorter in the treatment group than in the control group (37.9 .+-. 5.6 days vs 53.3 .+-. 8.3 days). Histological examination confirmed that bFGF stimulates the formation of granulation tissue, the regeneration of capillaries and the proliferation of fibroblasts. Immunohistochemical staining of the extracellular matrix of the granulation tissue showed that the amounts of fibronectin, laminin and type III collagen were higher in the treatment group. Heparin and gentamycin each enhanced the action of bFGF in wound healing. In order to maintain bFGF activity, it is essential that the wound track is kept free of infection and all necrotic tissue be excised.

L141 ANSWER 58 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97077286 EMBASE
DOCUMENT NUMBER: 1997077286
TITLE: Effects of fibroblast growth factor on the healing process of tympanic membrane perforations in an animal model.
AUTHOR: Ozkaptan Y.; Gerek M.; Simsek S.; Deveci S.
CORPORATE SOURCE: Y. Ozkaptan, Dept Otorhinolaryngol-Head Neck Surg, Gulhane Military Medical Academy, Etlik, TR-06018 Ankara, Turkey
SOURCE: European Archives of Oto-Rhino-Laryngology, (1997) 254/SUPPL. 1 (S2-S5).
Refs: 12
ISSN: 0937-4477 CODEN: EAOTE7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 011 Otorhinolaryngology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB After traumatic perforation of the tympanic membrane (TM), healing occurs spontaneously in most cases, although occasional perforations will fail to close. Healing of epithelia at any site involves cell movement, with

injury providing the stimulus to initiate changes in the behavior of cells that are normally static. Epidermal proliferation at the margins of the TM perforation can be accelerated by using such growth factors as epidermal growth factor, basic fibroblast growth factor (bFGF) and hyalorunan. bFGF is chemotactic and mitogenic for both fibroblasts and endothelial cells and is also mitogenic for keratinocytes. The effect of bFGF is significant in the enhancement of fibroblast production and angiogenesis. In this study, bFGF was used to enhance the healing process of chronic TM perforations in a guinea pig animal model. Chronic perforations were created since acute TMs could heal spontaneously without using any bioactive substance. In all, 30 TMs of 15 guinea pigs were used. A thermal myringotomy loop was employed to create a subtotal TM perforation at the area of the pars tensa. After establishing a permanent, non-infected perforation, bFGF in buffered saline solution was applied as 400 ng/day to 15 ears, while the opposite (control) ear was treated with only saline solution. At 20 days, 13 of 15 perforations treated with bFGF had closed. Light microscopy was used to assess organization of the healed TMs. The effects of bFGF on the healing process of TM perforations were compared in treated and non-treated ears.

L141 ANSWER 59 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95279311 EMBASE
DOCUMENT NUMBER: 1995279311
TITLE: TGP-580.
AUTHOR: Rabasseda X.; Mealy N.
CORPORATE SOURCE: Prous Science Publishers, P.O. Box 540,08080 Barcelona, Spain
SOURCE: Drugs of the Future, (1995) 20/8 (790-791).
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 008 Neurology and Neurosurgery
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L141 ANSWER 60 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95108863 EMBASE
DOCUMENT NUMBER: 1995108863
TITLE: Fibroblast growth factors in operative wound healing.
AUTHOR: Brew E.C.; Mitchell M.B.; Harken A.H.
CORPORATE SOURCE: Department of Surgery, Colorado Univ. Health Sciences Ctr., 4200 East Ninth Avenue,Denver, CO 80262, United States
SOURCE: Journal of the American College of Surgeons, (1995) 180/4 (499-504).
ISSN: 1072-7515 CODEN: JACSEX
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 009 Surgery
037 Drug Literature Index
LANGUAGE: English

L141 ANSWER 61 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95131239 EMBASE
DOCUMENT NUMBER: 1995131239
TITLE: Pharmacologic enhancement of wound healing.
AUTHOR: Pierce G.F.; Mustoe T.A.
CORPORATE SOURCE: Department of Preclinical Sciences, PRIZM Pharmaceuticals,San Diego, CA 92121, United States
SOURCE: Annual Review of Medicine, (1995) 46/- (467-481).
ISSN: 0066-4219 CODEN: ARMCAH
COUNTRY: United States

DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 013 Dermatology and Venereology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The field of pharmacologic modulation of soft tissue repair is in its infancy. Although the soluble, cellular, and insoluble mediators that govern repair have not been elucidated, the application of pharmacologic concentrations of purified polypeptide growth factors, cytokines, and matrix molecules has nonetheless resulted in the acceleration of normal repair and the reversal of deficient repair in a wide variety of dermal wound models in animals. However, early clinical results using these factors have been less than encouraging, and their potential roles in the armamentarium of chronic wound therapies remain to be established.

L141 ANSWER 62 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95297349 EMBASE
DOCUMENT NUMBER: 1995297349
TITLE: Stimulation of mucosal glutathione and angiogenesis: New mechanisms of gastroprotection and ulcer healing by sucralfate.
AUTHOR: Sandor Z.; Nagata M.; Kusstatscher S.; Szabo S.
CORPORATE SOURCE: Pathol./Lab. Medicine Service (113), VA Medical Center, 5901 East 7th Street,Long Beach, CA 90822-5201, United States
SOURCE: Scandinavian Journal of Gastroenterology, Supplement, (1995) 30/210 (19-21).
ISSN: 0085-5928 CODEN: SJGSB8
COUNTRY: Norway
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
029 Clinical Biochemistry
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background. Among the endogenous mediators (e.g., PG, SH) of gastroprotection, so far only PG was implicated in the mechanism of acute gastroprotection by sucralfate. Angiogenesis, which is stimulated by bFGF, is a recently recognized element in ulcer healing, and sucralfate binds bFGF in vitro and in vivo. Methods: In fasted rats the gastric mucosal concentration of GSH and protein SH was measured at 30, 60, 120, and 240 min after a single gastroprotective dose of sucralfate. In normally fed rats, angiogenesis was measured in the subcutaneous sponge assay 7 days after the implantation of sponges containing sucralfate and/or bFGF. Results: A gastroprotective dose of sucralfate time-dependently increased GSH concentration in the gastric mucosa. Sucralfate alone accelerated angiogenesis, which was significantly enhanced by combination with an ineffective dose of bFGF in the subcutaneous sponge assay. The same dose of sucralfate combined with an angiogenic dose of bFGF also resulted in synergistic stimulation (e.g., more than fivefold) of angiogenesis. Conclusions: It appears that elevated mucosal GSH concentration may represent a new factor in the mechanism of acute gastroprotection by sucralfate, and stimulation of angiogenesis is one of the mechanisms of ulcer healing by sucralfate.

L141 ANSWER 63 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95091691 EMBASE
DOCUMENT NUMBER: 1995091691
TITLE: Molecular and cellular basis of ulcer healing.
AUTHOR: Szabo S.; Kusstatscher S.; Sandor Z.; Sakoulas G.
CORPORATE SOURCE: Department of Pathology, Brigham and Women's Hospital,

SOURCE: Harvard Medical School, 75 Francis Street,Boston, MA 02115, United States
Scandinavian Journal of Gastroenterology, Supplement, (1995) 30/208 (3-8).
ISSN: 0085-5928 CODEN: SJGSB8

COUNTRY: Norway
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
048 Gastroenterology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: The high ulcer recurrence rates after treatment with antacids or antisecretory drugs illustrate the need for direct treatment of GI ulcers by stimulating repair and healing mechanisms. The molecular regulators of ulcer healing include polyamines and growth factors such as EGF, TGF-.beta., bFGF and PDGF. Methods and results: Oral treatment of rats with bFGF or PDGF accelerated the healing of chronic cysteamine-induced duodenal ulcers without decreasing gastric secretion. We found that sucralfate binds bFGF in vitro and in vivo, and the elevated local concentration of this growth factor may contribute to the ulcer healing properties of sucralfate. Parallel treatment with bFGF + sucralfate resulted in synergistic healing of chronic duodenal ulcers and chronic gastritis. Conclusions: Rapid changes in mucosal concentration of bFGF and EGF receptors during ulceration suggest that these peptides play a role in the natural history of GI ulcers. Thus, treatment based on molecular and cellular mechanisms of ulcer healing allows a direct and efficient ulcer therapy.

L141 ANSWER 64 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94117521 EMBASE
DOCUMENT NUMBER: 1994117521
TITLE: Accelerated healing of duodenal ulcers by oral administration of a mutein of basic fibroblast growth factor in rats.
AUTHOR: Szabo S.; Folkman J.; Vattay P.; Morales R.E.; Pinkus G.S.; Kato K.
CORPORATE SOURCE: Department of Pathology, Brigham and Women's Hospital, 75 Francis Street,Boston, MA 02115, United States
SOURCE: Gastroenterology, (1994) 106/4 (1106-1111).
ISSN: 0016-5085 CODEN: GASTAB

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
048 Gastroenterology

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background/Aims: Human basic fibroblast growth factor (bFGF) is an endothelial mitogen that stimulates angiogenesis and proliferation of other cells such as fibroblasts and smooth muscle cells. After this peptide was stabilized to acid and pepsin by site-specific mutagenesis, it was tested whether bFGF might accelerate the healing of experimental duodenal ulcers. Methods: This mutein peptide (bFGF-CS23) was administered orally in comparison with cimetidine to rats with chronic duodenal ulcers previously induced by cysteamine. Results: Oral bFGF-CS23 therapy maintained for 21 days at 100 ng/100 g twice daily resulted in (1) significant acceleration of healing of duodenal ulcers, i.e., reduction of mean ulcer area by 83% in the bFGF-CS23-treated rats compared with only 61% for cimetidine therapy and 40% for untreated controls; (2) complete healing with no residual ulcer in 62% of the bFGF-CS23-treated rats compared with only 7% of untreated rats; and (3) a ninefold increase in angiogenesis in the ulcer bed compared with untreated controls. A single dose of the bFGF-CS23 mutein had no effect on gastric output of

hydrochloric acid or pepsin, but daily treatment for 2 or 3 weeks resulted in enhanced acid and pepsin outputs. Conclusions: Chronic duodenal ulcers can be healed rapidly by stimulating angiogenesis and other wound- healing processes in the ulcer bed without reduction of gastric acid.

L141 ANSWER 65 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94180271 EMBASE
DOCUMENT NUMBER: 1994180271
TITLE: Omentum and basic fibroblast growth factor in healing of chronic gastric ulcerations in rats.
AUTHOR: Konturek S.J.; Brzozowski T.; Majka I.; Pawlik W.; Stachura J.
CORPORATE SOURCE: Institute of Physiology, University Medical School, ul. Grzegorzecka 16,31-531 Krakow, Poland
SOURCE: Digestive Diseases and Sciences, (1994) 39/5 (1064-1071). ISSN: 0163-2116 CODEN: DDSCDJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
048 Gastroenterology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Omentum was shown to exhibit angiogenic activity, but its role in healing of chronic gastric ulcers is unknown. This study was designed to compare the effects of omentum and basic fibroblast growth factor (bFGF), a potent angiogenic factor, on healing of chronic gastric ulcers in rats. Several series of rats with gastric ulcers were used: series A with intact omentum (control), series B with omentum resected, and series C with omentum placed on the serosal side of the ulcer. Series A-C were divided into four groups treated with vehicle (I); indomethacin (II), an inhibitor of prostaglandin formation, difluoromethylornithine (DFMO) (III); an inhibitor of polyamine biosynthesis or bFGF (IV). Seven days after ulcer induction, the animals were anesthetized, the gastric blood flow (GBF) was determined by laser Doppler flowmetry (LDF), and the ulcer area was measured by planimetry. Biopsy samples of the ulcer margin were taken for determination of the number of capillaries and myofibroblasts in the granulation tissue. Attachment of omentum significantly accelerated ulcer healing, whereas omentectomy delayed this process. LDF revealed the decrease in the GBF at the ulcer margin to 45% and at the ulcer bed to 18% of the value recorded in the intact adjacent mucosa. Attachment of the omentum significantly increased the blood flow at the ulcer margin and increased the number of capillaries and myofibroblasts in the granulation tissue. Indomethacin (1 mg/kg/day) that inhibited mucosal PGE2 by about 85% delayed significantly ulcer healing without affecting the blood flow in the ulcer area. DFMO (200 mg/kg intraperitoneally) suppressed ODC activity in the mucosa but did not influence the ulcer healing. bFGF given subcutaneously accelerated dose-dependently ulcer healing and stimulated angiogenesis to a similar extent as the attached omentum. We conclude that omentum enhances the ulcer healing in similar way as bFGF and that this effect is accompanied by the increased angiogenesis and blood flow in the ulcer area.

L141 ANSWER 66 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93267163 EMBASE
DOCUMENT NUMBER: 1993267163
TITLE: Cultured ocular cells and extracellular matrices: Role of growth factors, retinoic acid and cell polarity.
AUTHOR: Kennedy A.; Frank R.N.
CORPORATE SOURCE: The Kresge Eye Institute, Wayne State University, School of Medicine, 4717 St Antoine Boulevard,Detroit, MI 48201, United States
SOURCE: Current Eye Research, (1993) 12/8 (693-702).

ISSN: 0271-3683 CODEN: CEYRDM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Culture of various types of cells on gelled, reconstituted extracellular matrices results in decreased cellular proliferation. In the present study, we evaluated several possible mechanisms for this inhibition, as applied to cultured bovine retinal microvascular endothelial cells (EC) or to retinal pigment epithelial (RPE) cells: whether the inhibition might be related to (a) inactivation of fibroblast growth factor (FGF) by binding of the molecules present in the medium to a matrix **component**; (**b**) release of an inhibitor by the matrix in culture; or (c) inhibitory properties of the matrix macromolecules themselves. Our results suggest that mechanism (c) is most likely. The reasons are, first, that culture of EC or RPE cells on several different extracellular matrix substrates in the presence of logarithmically increasing concentrations of acidic or basic fibroblast growth factors (aFGF or bFGF) leads to a vertical shift of the plots of cell number after 4 days in culture vs. log growth factor concentration for both types of cells. The same result obtains when cells are cultured with logarithmically increasing concentrations of all-trans retinoic acid, which inhibits EC but not RPE cell proliferation in a dose-dependent fashion. This is consistent with mechanism (b) or (c), but not (a), for which one would expect a horizontal shift. Second, washing the matrices prior to the plating of cells with 1M NaCl, which elutes aFGF and partially elutes bFGF molecules from basement membranes, does not alter the growth of cells plated after the wash. This suggests also that growth factor binding to the matrix is not a likely mechanism for the observed inhibition. Incubation of matrices with culture medium prior to plating cells does not usually alter the ability of the medium thus 'conditioned' to support cell growth, arguing against the possibility that the matrices release a soluble activator or inhibitor of such growth. However, in some experiments performed with lots of Matrigel.RTM.) (a commercially available basement membrane extract from a murine tumor) obtained prior to mid-1991, media 'conditioned' by incubation with this matrix did show enhanced ability to facilitate F,C and RPE cell proliferation. Finally, if RPE cells or EC are plated on various substrates, allowed to attach for 24 hr., and then the same or other substrates are poured over the cells, the effect on proliferation of the matrices plated on the apical surfaces of the cells is often less than that of matrices plated adjacent to their basal surfaces. Although in most cases these differences are not statistically significant, there is an apparent trend. The overall results of this experiment suggest an asymmetrical cell-substrate interaction, mediated through receptors located predominantly on the basal surfaces of the cells.

L141 ANSWER 67 OF 83 EMBASE
ACCESSION NUMBER: 93079283 EMBASE
DOCUMENT NUMBER: 1993079283
TITLE: Axonal transport and morphological changes following nerve compression. An experimental study in the rabbit vagus nerve.
AUTHOR: Dahlin L.B.; Archer D.R.; McLean W.G.
CORPORATE SOURCE: Department of Hand Surgery, General Hospital, Lund University,S-214 01 Malmo, Sweden
SOURCE: Journal of Hand Surgery, (1993) 18 B/1 (106-110).
ISSN: 0266-7681 CODEN: JHASE4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy

008 Neurology and Neurosurgery
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Axonal transport and morphological changes were studied in the rabbit vagus nerve after the nerves had been subjected to compression at either 0, 50 or 200 mmHg for two hours. Slow axonally transported proteins, tubulin and actin, were radiolabelled with 35S-methionine two, seven or 14 days after the injury and the distribution of radiolabelled tubulin and actin within **component b** of slow transport was measured three days later by densitometric analysis of fluorographs of polyacrylamide gel. No significant differences were found in the distribution of tubulin two (50 and 200 mmHg) or seven (200 mmHg) days after injury, but at 14 days (200 mmHg) there was significantly increased radiolabelling of tubulin relative to actin in the nerve 60 to 70 mm from the nodose ganglion. Morphometric measurements of the nerve cell bodies two days after the compression injury at 200 mmHg revealed no significant changes. Previous work has shown that morphological changes, similar to those found after axotomy, were present in nerve cell bodies seven days after a compression injury. This, taken together with the present results, indicates that compression can induce both morphological and biochemical changes in the neurone. The altered axonal transport of tubulin associated with nerve injury follows a slower time course and does not precede the morphological changes. The findings may be of relevance when discussing the double crush syndrome.

L141 ANSWER 68 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92083678 EMBASE
DOCUMENT NUMBER: 1992083678
TITLE: Basic fibroblast growth factor in retardation of doxorubicin extravasation injury.
AUTHOR: Vasilev S.A.; Morrow C.; Morrow C.P.
CORPORATE SOURCE: Division of Surgery, Dept. of Gynecologic Oncology, City of Hope Natl. Med. Ctr., 1500 E. Duarte Rd.,Duarte, CA 91010, United States
SOURCE: Gynecologic Oncology, (1992) 44/2 (178-181).
ISSN: 0090-8258 CODEN: GYNOA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Extravasation of chemotherapeutic agents such as doxorubicin results in significant morbidity and remains a serious clinical problem. No single agent or combination of agents has proven to be completely effective in preventing the chronic avascular ulcerative wound. Basic fibroblast growth factor (bFGF) is one of many angiogenic agents and is strongly mitogenic for vascular endothelial cells in nanogram quantities. In a Sprague-Dawley rat model, bFGF was moderately effective in retarding the development of doxorubicin-induced skin ulceration.

L141 ANSWER 69 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91103869 EMBASE
DOCUMENT NUMBER: 1991103869
TITLE: Conditioning nerve crush accelerates cytoskeletal protein transport in sprouts that form after a subsequent crush.
AUTHOR: McQuarrie I.G.; Jacob J.M.
CORPORATE SOURCE: Neural Regeneration Center, Veterans Affairs Medical Ctr., 10701 East Blvd.,Cleveland, OH 44106, United States
SOURCE: Journal of Comparative Neurology, (1991) 305/1 (139-147).

ISSN: 0021-9967 CODEN: JCNEAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB To examine the relationship between axonal outgrowth and the delivery of cytoskeletal proteins to the growing axon tip, outgrowth was accelerated by using a conditioning nerve crush. Because slow **component b** (SCb) of axonal transport is the most rapid vehicle for carrying cytoskeletal proteins to the axon tip, the rate of SCb was measured in conditioned vs. sham-conditioned sprouts. In young Sprague-Dawley rats, the conditioning crush was made to sciatic nerve branches at the knee; 14 days later, the test crush was made where the L4 and L5 spinal nerves join to form the sciatic nerve in the flank. Newly synthesized proteins were labeled in motor neurons by injecting 35S-methionine into the lumbar spinal cord 7 days before the test crush. The wave of pulse-labeled SCb proteins reached the crush by the time it was made and subsequently entered sprouts. The nerve was removed and sectioned for SDS-PAGE and fluorography 4-12 days after the crush. Tubulins, neurofilament proteins, and representative 'cytomatrix' proteins (actin, calmodulin, and putative microtubule-associated proteins) were removed from gels for liquid scintillation counting. Labeled SCb proteins entered sprouts without first accumulating in parent axon stumps, presumably because sprouts begin to grow within hours after axotomy. The peak of SCb moved 11% faster in conditioned than in sham-conditioned sprouts: 3.0 vs. 2.7 mm/d ($p < 0.05$). To confirm that sprouts elongate more rapidly when a test crush is preceded by a conditioning crush, outgrowth distances were measured in a separate group of rats by labeling fast axonal transport with 3H-proline 24 hours before nerve retrieval. The rate of outgrowth was 17% faster in conditioned than in sham-conditioned sprouts: 5.13 vs. 4.38 mm/d ($p < 0.01$). The increase in outgrowth rate correlated with the increase in SCb rate, suggesting that outgrowth is a function of cytoskeletal protein transport.

L141 ANSWER 70 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90255893 EMBASE
DOCUMENT NUMBER: 1990255893
TITLE: Effect of orally administered bFGF on acute and chronic duodenal ulcers, gastric secretion and acute mucosal lesions in rats.
AUTHOR: Szabo S.; Folkman J.; Vattay P.; Morales R.E.; Pinkus G.; Kato K.
CORPORATE SOURCE: Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, United States
SOURCE: European Journal of Pharmacology, (1990) 183/6 (2090). ISSN: 0014-2999 CODEN: EJPHAZ
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L141 ANSWER 71 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 84132713 EMBASE
DOCUMENT NUMBER: 1984132713
TITLE: Identification of Thormahlen-positive **compound** ' **B**' in **urine** of patients with malignant melanoma.
AUTHOR: Pavel S.; Boverhof R.; Van der Slik W.
CORPORATE SOURCE: Central Laboratory for Clinical Chemistry, University

Hospital, NL-9700 RB Groningen, Netherlands
SOURCE: Archives of Dermatological Research, (1984) 276/3 (156-159).
CODEN: ADMFAU
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
AB The identification of the entire structure of the Thormahlen-positive **compound B** from melanotic **urine** is described.
The compound was separated from other Thormahlen-positive compounds using DEAE-cellulose column chromatography. On the basis of differential enzymic hydrolysis followed by gas chromatography-mass spectrometry analysis and comparison with synthetically prepared compounds it is possible to conclude that the Thormahlen-positive **compound B** is a mixture of O-sulphate 5-hydroxy-6-methoxyindole and 6-hydroxy-5-methoxyindole with predominance of the latter.

L141 ANSWER 72 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 82186893 EMBASE
DOCUMENT NUMBER: 1982186893
TITLE: Puncture of thoracic lesions under sonographic guidance.
AUTHOR: Afschrift M.; Nachtegaele P.; Voet D.; et al.
CORPORATE SOURCE: Dep. Intern. Med., Akad. Ziekenh., Ghent, Belgium
SOURCE: Thorax, (1982) 37/7 (503-506).
CODEN: THORA7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
014 Radiology
016 Cancer
009 Surgery
LANGUAGE: English
AB Thirty-six punctures of thoracic lesions have been performed with a **compound B**-scanner or a real-time linear-array scanner for guidance. Twenty-three fluid collections were punctured and aspiration biopsies were performed on 13 echogenic lesions. All the punctures were successful at the first attempt. No complications occurred. The results confirm the usefulness of sonography for guiding punctures of thoracic fluid effusions and solid masses. Usually a static B-scanner is sufficient, but when masses are small or surrounded by vital structures puncture may be controlled by a real-time scanner.

L141 ANSWER 73 OF 83 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 78398061 EMBASE
DOCUMENT NUMBER: 1978398061
TITLE: Undetected brain damage in Irish alcoholics.
AUTHOR: Draper R.J.; Feldman B.; Haughton H.
CORPORATE SOURCE: St. Patrick's Hosp., Dublin, Ireland
SOURCE: Irish Medical Journal, (1978) 71/10 (353-355).
CODEN: IMDJBD
COUNTRY: Ireland
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
017 Public Health, Social Medicine and Epidemiology
049 Forensic Science Abstracts
032 Psychiatry
008 Neurology and Neurosurgery
LANGUAGE: English
AB The full range of defects appear to occur frequently in Irish alcoholics and persists even with prolonged abstinence although Haughton (1978) found

evidence that partial recovery may occur in some areas, notable visual memory. There appear to be two components to the syndrome (a) a recoverable cerebral dysfunction **component**, (**b**) a persistent brain damage component, based upon demonstrable cortical atrophy. It has been a matter of choice and degree of severity whether a cerebral dysfunction or brain-damage label has been used. The latter term appears to be fully justified. Society must face the fact that every day Irish men and women are suffering permanent brain damage as a result of their use of alcohol. These people are not some band of skid row types to be comfortably dismissed with a 'couldn't happen to me' posture. They are ordinary people, neighbours, colleagues, relatives. They are drawn from every occupation, every social group. Most will be working, many in positions of responsibility. They will hazard not only their own health and safety but that of others. Once brain damage develops they will be a risk whether intoxicated or sober. Alcoholism accounts for one quarter of all Irish psychiatric admissions. Its protean behavioural and physical manifestations have been widely reported. This paper draws attention to another sinister complication, which has been demonstrated to occur in Irish drinkers and which lurks undetected in the shadows until irretrievable loss of function has already started to occur.

L141 ANSWER 74 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-515596 [47] WPIDS
DOC. NO. CPI: C2000-153904
TITLE: Hydrogel comprising protein or enzyme bonded to PEG via urea groups, useful as a dressing for **wounds** and burns.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): ETTNER, N; MEIER, W; SAUER, M; SCHINK, M; SCHREIBER, J
PATENT ASSIGNEE(S): (BEIE) BEIERSDORF AG
COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 19903655	A1	20000810	(200047)*		18
AU 9963077	A	20000803	(200047)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 19903655	A1	DE 1999-19903655	19990129
AU 9963077	A	AU 1999-63077	19991203

PRIORITY APPLN. INFO: DE 1999-19903655 19990129
AB DE 19903655 A UPAB: 20000925
NOVELTY - A hydrogel formed from a protein and/or enzyme and/or SOD/catalase enzyme mimic bonded to a PEG via urea groups is new.

DETAILED DESCRIPTION - The hydrogel consists of (A) at least one protein and/or enzyme and/or SOD/catalase enzyme mimic (including protein and enzyme fragments and/or recombinantly produced forms) bonded to (B) a PEG via urea groups.

An INDEPENDENT CLAIM is also included for the preparation of the hydrogel.

USE - The hydrogel is useful as a dressing for **wounds**, especially deep and superficial severe **wounds**, and burns.

ADVANTAGE - Compared with currently available biosynthetic hydrogels, the hydrogels form gels with water in a shorter time. Also, they avoid problems associated with the formation of p-nitrophenols as cleavage products in the hydrogel matrix and the possible defective bonding of oligomeric proteins.

Dwg.0/2

L141 ANSWER 75 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-395094 [33] WPIDS
DOC. NO. CPI: C1999-116133
TITLE: Pharmaceutical composition, especially for gene transfer and therapy.
DERWENT CLASS: A96 A97 B04 B05 D16
INVENTOR(S): BERNDT, A; RESZKA, R
PATENT ASSIGNEE(S): (DELB-N) DELBRUECK CENT MOLEKULARE MEDIZIN MAX
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9930741	A2	19990624	(199933)*	GE	28
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
DE 19859526	A1	19990819	(199939)		
EP 1037670	A2	20000927	(200048)	GE	
R: AT BE CH DE DK FI FR GB IT LI NL SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9930741	A2	WO 1998-DE3763	19981214
DE 19859526	A1	DE 1998-19859526	19981214
EP 1037670	A2	EP 1998-966568	19981214
		WO 1998-DE3763	19981214

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1037670	A2	Based on	WO 9930741

PRIORITY APPLN. INFO: DE 1997-19756309 19971212

AB WO 9930741 A UPAB: 19990819
NOVELTY - A pharmaceutical composition comprising genetic material optionally encapsulated in liposomes as well as starch particles and/or gelatine and/or polymer particles and a contrast agent is new.

DETAILED DESCRIPTION - A pharmaceutical composition comprises:

(a) genetic material(s) optionally encapsulated in PEG, immuno, immuno/PEG, cationic or optionally polymer-modified liposomes;

(b) lyophilized or degradable starch particles and/or gelatine and/or polymer particles, e.g. nanoparticles; and

(c) a contrast agent containing iodine, gadolinium, magnetite or fluorine.

The composition can also conveniently contain DNA density-packing proteins, e.g. Nuclear Capsid Protein (NCP 7), HMG and/or synthetic substances, e.g. polyethyleneimine, poly-L-lysine or protamine sulphate.

An INDEPENDENT CLAIMS is also included for the preparation of the composition.

ACTIVITY - Nootropic; Neuroprotective; Antidiabetic; Vasotropic; Hypotensive.

MECHANISM OF ACTION - None given.

USE - The composition is useful for gene transfer and therapy, especially for the treatment, particularly local, of liver metastases, glioblastoma, tumors of the lung, bladder, head and neck, genitalia, lymph nodes and breast as well as arthritis and asthma. The composition is also useful for the treatment of neurogenerative and autoimmune disease, e.g. Parkinson's and Alzheimer's diseases, multiple sclerosis and type I

diabetes. Also, the composition can be used as an aid in transplants and for the treatment of restenosis as well as hypertension associated with the latter.

ADVANTAGE - The composition provides a new approach to local-regional therapy of tumors, especially liver metastases, and avoids the low tumor specificity and high toxicity of known chemotherapeutics.

Dwg.0/1

L141 ANSWER 76 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-106209 [09] WPIDS
DOC. NO. NON-CPI: N1999-076606
DOC. NO. CPI: C1999-031838
TITLE: Identifying compounds which modify Smad signalling pathways - used to identify compounds for treating e.g. cancers, fibrosis, Alzheimer's disease, memory loss, inflammation, immunoregulation or atherosclerosis.
DERWENT CLASS: B03 B04 D16 S03
INVENTOR(S): MASSAGUE, J; PAVLETICH, N; SHI, Y
PATENT ASSIGNEE(S): (SLOK) SLOAN KETTERING INST CANCER RES
COUNTRY COUNT: 70
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9901765	A1	19990114	(199909)*	EN	179
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL OA PT SE					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN					
AU 9882813	A	19990125	(199923)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9901765	A1	WO 1998-US13721	19980701
AU 9882813	A	AU 1998-82813	19980701

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9882813	A	Based on	WO 9901765

PRIORITY APPLN. INFO: US 1997-65113P 19971112; US 1997-52774P 19970701

AB WO 9901765 A UPAB: 19990302

A method of testing compounds comprises: (a) providing a Smad4 polypeptide comprising the L3 loop region, a complementary Smad polypeptide, and a compound to be tested; (b) contacting the Smad4 polypeptide with the complementary Smad polypeptide where binding can take place, where the contacting is performed in the presence and absence of the compound; and (c) detecting an increase or decrease in binding of the Smad4 polypeptide to the complementary Smad polypeptide in the presence of the compound. Also claimed are: (1) a method of testing compounds, comprising: (a) providing 2 Smad polypeptides from the same Smad family comprising the C-terminal domains of each, and a compound to be tested; (b) contacting the Smad polypeptides where binding can take place, where the contacting is performed in the presence and absence of the compound; and (c) detecting an increase or decrease in binding of the Smad polypeptides to each other in the presence of the compound; (2) a method of testing compounds comprising: (a) providing a Smad polypeptide comprising the C-terminal domain, a polypeptide comprising the L45 loop of the kinase

domain corresponding to a receptor of the transforming **growth factor** (TGF)- beta or bone morphogenic protein (BMP) family, and a test **compound**; (**b**) contacting the Smad polypeptide with the receptor polypeptide where phosphorylation can take place, where the contacting is performed in the presence and absence of the compound; and (c) detecting an increase or decrease in the phosphorylation of the Smad polypeptide in the presence of the compound; (3) a method of testing compounds comprising: (a) providing a Smad polypeptide comprising the alpha -helix 2 of the MH2 domain, a DNA binding polypeptide, and a compound to be tested; and (b) contacting the Smad polypeptide with the DNA binding polypeptide where binding can take place, where the contacting is performed in the presence and absence of the compound; and (c) detecting whether there is an increase in binding of the Smad polypeptide to the DNA binding polypeptide in the presence of the compound; (4) a method of testing compounds, comprising: (a) providing 2 Smad polypeptides comprising the C-terminus of each, a Smad polypeptide comprising the N-terminal domain, and a compound to be tested; and (b) contacting the Smad C-terminus polypeptides in the presence of the Smad N-terminal domain where binding can take place, where the contacting is performed in the presence and absence of the compound; (c) detecting whether there is an increase or decrease in binding of the Smad C-terminus domains in the presence of the compound due to inhibition of the autoinhibitory function of the N-terminal domain by the compound, and (5) a method of testing compounds comprising: (a) providing a Smad polypeptide comprising the C-terminal domain, a polypeptide comprising the L45 loop of the kinase domain corresponding to a receptor of the TGF- beta or BMP family, and a test **compound**; (**b**) contacting the Smad polypeptide with the receptor polypeptide where binding can take place, where the contacting is performed in the presence and absence of the compound; and (c) detecting an increase or decrease in the binding of the Smad polypeptide to the kinase domain in the presence of the compound.

USE - The compounds which enhance the Smad signalling pathway can be used in the treatment of cancers while compounds that inhibit the pathway would be beneficial in the treatment of fibrosis. The compounds identified can be used in the treatment of pancreatic cancer, breast cancer, ovarian cancer, colon cancer, esophageal cancer, head and neck cancers, fibrosis of the kidney, fibrosis of the liver, fibrosis of the lung, Alzheimer's disease, memory loss, inflammation, **wound** healing, bone growth, immunoregulation, blood cell formation and atherosclerosis (claimed). Dwg.0/24

L141 ANSWER 77 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-032143 [03] WPIDS
DOC. NO. CPI: C1998-010789
TITLE: Composition useful as **cicatrizant** - comprises **component B**, used for treatment of **wounds**, **ulcers** and other traumatic lesions.
DERWENT CLASS: B04
INVENTOR(S): BORRELLI, F; DONINI, S; MARTELLI, F; MASTRANGELI, R; FABRIZIO, M; FRANCESCO, B; RENATO, M; SILVIA, D
PATENT ASSIGNEE(S): (ISTF) ARS APPLIED RES SYSTEMS HOLDING NV
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9739765	A1	19971030	(199803)*	JA	44
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP KR NO UA US					
AU 9657605	A	19971112	(199811)		
ZA 9703442	A	19980429	(199822)		42
NO 9804965	A	19981201	(199907)		

EP 895478 A1 19990210 (199911) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5998364 A 19991207 (200004)
JP 2000510436 W 20000815 (200044) 44
KR 2000005414 A 20000125 (200063)
AU 727618 B 20001214 (200103)#
IL 120696 A 20011031 (200174)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9739765	A1	WO 1996-EP1702	19960424
AU 9657605	A	AU 1996-57605	19960424
		WO 1996-EP1702	19960424
ZA 9703442	A	ZA 1997-3442	19970422
NO 9804965	A	WO 1996-EP1702	19960424
		NO 1998-4965	19981023
EP 895478	A1	EP 1996-914107	19960424
		WO 1996-EP1702	19960424
US 5998364	A	WO 1996-EP1702	19960424
		US 1999-171659	19990127
JP 2000510436	W	WO 1996-EP1702	19960424
		JP 1997-506037	19960424
KR 2000005414	A	WO 1996-EP1702	19960424
		KR 1998-708151	19981013
AU 727618	B	AU 1996-57605	19960424
IL 120696	A	IL 1997-120696	19970417

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9657605	A	Based on	WO 9739765
EP 895478	A1	Based on	WO 9739765
US 5998364	A	Based on	WO 9739765
JP 2000510436	W	Based on	WO 9739765
KR 2000005414	A	Based on	WO 9739765
AU 727618	B	Previous Publ.	AU 9657605
		Based on	WO 9739765

PRIORITY APPLN. INFO: WO 1996-EP1702 19960424
AB WO 9739765 A UPAB: 19980119
Composition useful as **cicatrizant** comprises **component B** (an 81-amino acid protein originally isolated from human **urine**, see WO 9414259) as the active ingredient.
USE - The compositions are useful for the treatment of **wounds**, **ulcers** and other traumatic lesions to any of the tissues in the body (claimed).
Dwg.0/10

L141 ANSWER 78 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994-234696 [28] WPIDS
DOC. NO. CPI: C1994-106819
TITLE: New protein, **component B**, isolated from **urine** - with antiinflammatory, anticoagulant and anti-tumour activities, also related nucleic acid, vectors and transformed cells..
DERWENT CLASS: A96 B04 D16
INVENTOR(S): SIRNA, A; SIMA, A
PATENT ASSIGNEE(S): (ISTF) ARS APPLIED RES SYSTEMS HOLDING NV; (ISTF) ARS APPLIED RES SYST HOLDING NV
COUNTRY COUNT: 29

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9414959	A1	19940707	(199428)*	EN	55
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU BY CA FI JP KR KZ NO RU UA US					
AU 9458335	A	19940719	(199439)		
FI 9503091	A	19950621	(199538)		
ZA 9309621	A	19950830	(199540)		68
NO 9502494	A	19950821	(199544)		
EP 675956	A1	19951011	(199545)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
IT 1257184	B	19960110	(199629)		
JP 08509359	W	19961008	(199705)		64
AU 690093	B	19980423	(199828)		
US 5908827	A	19990601	(199929)		
JP 3025014	B2	20000327	(200020)		34
KR 193107	B1	19990615	(200059)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9414959	A1	WO 1993-EP3645	19931221
AU 9458335	A	AU 1994-58335	19931221
FI 9503091	A	WO 1993-EP3645	19931221
		FI 1995-3091	19950621
ZA 9309621	A	ZA 1993-9621	19931222
NO 9502494	A	WO 1993-EP3645	19931221
		NO 1995-2494	19950621
EP 675956	A1	WO 1993-EP3645	19931221
		EP 1994-904167	19931221
IT 1257184	B	IT 1992-RM919	19921222
JP 08509359	W	WO 1993-EP3645	19931221
		JP 1994-514813	19931221
AU 690093	B	AU 1994-58335	19931221
US 5908827	A	WO 1993-EP3645	19931221
		US 1996-448561	19960122
JP 3025014	B2	WO 1993-EP3645	19931221
		JP 1994-514813	19931221
KR 193107	B1	WO 1993-EP3645	19931221
		KR 1995-702407	19950613

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9458335	A	Based on	WO 9414959
EP 675956	A1	Based on	WO 9414959
JP 08509359	W	Based on	WO 9414959
AU 690093	B	Previous Publ.	AU 9458335
		Based on	WO 9414959
US 5908827	A	Based on	WO 9414959
JP 3025014	B2	Previous Publ.	JP 08509359
		Based on	WO 9414959

PRIORITY APPLN. INFO: IT 1992-RM919 19921222

AB WO 9414959 A UPAB: 19940831

Polypeptide (I), designated **component B** or its salts, functional derivs., precursors and/or active fragments are new.

Also new are (1) DNA encoding (I), its mutants and active fragments, also DNA hybridising with this, (2) expression vectors contg. such DNA and

(3) host cells transformed with these vectors. The specification includes the sequences of the genomic transcriptional unit of (I) (about 1400 bp, 103 amino acids including the 22 amino acid signal sequence), also the sequences of the 577 promoter region.

(I) is isolated from **urine** (esp. human) by adsorption at acid pH on kaolin, then extn. with NH4OH. The extract is then chromatographed sequentially on 'Bio Rex 70' resin (NH4OH), DEAE Sepharose (acetate buffer), CM Sepharose (acetate buffer), HPLC C18 (acetate buffer/MeCN), DE-52 resin (acetate buffer), D-Zephyr resin (acetate buffer), HPLC C18 (aq. CF3COOH/MeCN) and D-Zephyr resin (acetate buffer).

USE - (I) inhibits binding of TGF-alpha to its receptor, so has antiinflammatory, anticoagulant and/or antitumour activities. It can also be used to treat conditions associated with altered levels of TGF-alpha, e.g. behavioural or hormonal disturbances and **angiogensis**. (I) is admin. orally, rectally, nasal, topically or esp. parenterally. It can also be released slowly from subcutaneous implants.

Dwg.6/8

L141 ANSWER 79 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994-035006 [04] WPIDS
CROSS REFERENCE: 1990-193414 [25]; 1995-208225 [28]; 1995-208226 [28]; 1995-375181 [49]; 1996-130504 [14]; 1997-022861 [03]; 1998-494612 [42]
DOC. NO. CPI: C1994-016178
TITLE: Non-immunogenic biocompatible polymer conjugates - used for soft tissue augmentation and for coating or forming various articles.
DERWENT CLASS: A96 B04 D22 P32 P81
INVENTOR(S): BENTZ, H; BERG, R A; BURNS, R A; DAMANI, R; DELUSTRO, F; FRIES, L; MCCULLOUGH, K; MICHAELS, A S; RHEE, W; WALLACE, D G
PATENT ASSIGNEE(S): (CLGE) COLLAGEN CORP
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9401483	A1	19940120	(199404)*	EN	101
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU JP					
US 5292802	A	19940308	(199410)		19
US 5308889	A	19940503	(199417)		23
AU 9346620	A	19940131	(199422)		
US 5324775	A	19940628	(199425)		22
US 5328955	A	19940712	(199427)		17
EP 648239	A1	19950419	(199520)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
US 5413791	A	19950509	(199524)		17
US 5446091	A	19950829	(199540)		16
US 5550188	A	19960827	(199640)		19
JP 08502082	W	19960305	(199644)		92
AU 677789	B	19970508	(199727)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9401483	A1		WO 1993-US6292	19930701
US 5292802	A	CIP of	US 1988-274071	19881121
		CIP of	US 1989-433441	19891114
		CIP of	US 1992-922541	19920730
			US 1992-985680	19921202
US 5308889	A	CIP of	US 1988-274071	19881121

		CIP of	US 1989-433441	19891114
		CIP of	US 1992-922541	19920730
			US 1992-984197	19921202
AU 9346620	A		AU 1993-46620	19930701
US 5324775	A	CIP of	US 1988-274071	19881121
		CIP of	US 1989-433441	19891114
			US 1992-907518	19920702
US 5328955	A	CIP of	US 1988-274071	19881121
		CIP of	US 1989-433441	19891114
			US 1992-922541	19920730
EP 648239	A1		EP 1993-916926	19930701
			WO 1993-US6292	19930701
US 5413791	A	CIP of	US 1988-274071	19881121
		CIP of	US 1989-433441	19891114
		Div ex	US 1992-922541	19920730
			US 1994-198128	19940217
US 5446091	A	CIP of	US 1988-274071	19881121
		CIP of	US 1989-433441	19891114
		Div ex	US 1992-922541	19920730
		Div ex	US 1994-198128	19940217
			US 1995-368874	19950105
US 5550188	A	CIP of	US 1988-274071	19881121
		CIP of	US 1989-433441	19891114
		Div ex	US 1992-922541	19920730
		Div ex	US 1994-198128	19940217
		Div ex	US 1995-368874	19950105
			US 1995-478510	19950607
JP 08502082	W		WO 1993-US6292	19930701
			JP 1994-503427	19930701
AU 677789	B		AU 1993-46620	19930701

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 5292802	A	CIP of	US 5162430
US 5308889	A	CIP of	US 5162430
AU 9346620	A	Based on	WO 9401483
US 5324775	A	CIP of	US 5162430
US 5328955	A	CIP of	US 5162430
EP 648239	A1	Based on	WO 9401483
US 5413791	A	CIP of	US 5162430
		Div ex	US 5328955
US 5446091	A	CIP of	US 5162430
		Div ex	US 5328955
		Div ex	US 5413791
US 5550188	A	CIP of	US 5162430
		Div ex	US 5328955
		Div ex	US 5413791
		Div ex	US 5446051
JP 08502082	W	Based on	WO 9401483
AU 677789	B	Previous Publ.	AU 9346620
		Based on	WO 9401483

PRIORITY APPLN. INFO: US 1993-25032 19930302; US 1992-907518 19920702; US 1992-922541 19920730; US 1992-984197 19921202; US 1992-984933 19921202; US 1992-985680 19921202; US 1988-274071 19881121; US 1989-433441 19891114; US 1994-198128 19940217; US 1995-368874 19950105; US 1995-478510 19950607

AB WO 9401483 A UPAB: 19981021

A biocompatible, biologically inert conjugate (C) comprises a natural

polymer or its deriv. chemically conjugated by an ether bond to a synthetic hydrophilic polymer.

Further claimed is a method for augmenting tissue in a mammal comprising admin. of a compsn. contg. an aq. mixt. of a natural polymer or its deriv. and an aq. compsn. of synthetic, non-immunogenic, hydrophilic polymer having a reactive gp. capable of forming a covalent ether bond in situ with the natural polymer, before crosslinking occurs between the natural and the synthetic polymer.

USE/ADVANTAGE - The conjugates and their compsns. can be combined with cytokines or growth factors to promote tissue growth and/or with other materials to increase the structural integrity of the compsns. so that they can be used in the augmentation of hard tissue, such as bone and cartilage. The conjugates can also be used as coatings for medical devices including catheters, bone implants and platinum wires to treat aneurysms. The covalent bonds in the conjugates can be used to provide a high degree of stability over long periods of time. The ether linkage used to connect the natural and synthetic polymers is resistant to breakage due to hydrolysis. The conjugates can be formed using a variety of natural and synthetic polymers, enabling the physical and chemical characteristics of the compsn. to be adjusted.

Dwg.0/17

L141 ANSWER 80 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1992-007482 [01] WPIDS
TITLE: Yeast derived compsn. similar to epidermal **growth factor** - promotes healing of burns, **wounds** and **ulcers** and prepd. more easily than by genetic engineering.
DERWENT CLASS: B04 D16
INVENTOR(S): KELLER, S J; LEVIN, R H
PATENT ASSIGNEE(S): (LEVI-I) LEVIN R H; (KELL-I) KELLER S J
COUNTRY COUNT: 4
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9118999	A	19911212	(199201)*		
AU 9179823	A	19911231	(199215)		
EP 497928	A1	19920812	(199233)	EN	36
US 5219998	A	19930615	(199325)		15
CA 2074156	A	19940118	(199414)#		
US 5397770	A	19950314	(199516)		14
IL 98234	A	19961114	(199705)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 497928	A1		EP 1991-911135	19910517
			WO 1991-US3491	19910517
US 5219998	A	CIP of	US 1990-534026	19900604
			US 1991-665997	19910307
CA 2074156	A		CA 1992-2074156	19920717
US 5397770	A	CIP of	US 1990-534026	19900604
		Div ex	US 1991-665997	19910307
			US 1993-21331	19930223
IL 98234	A		IL 1991-98234	19910523

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 497928	A1	Based on	WO 9118999

US 5397770 A Div ex US 5219998

PRIORITY APPLN. INFO: US 1990-534026 19900604; US 1991-665997 19910307

AB WO 9118999 A UPAB: 19931006

A yeast-derived epidermal **growth factor** (EGF)-like compsn. (A) having an equivalency of at least 1000ng of mouse-derived EGF activity/mg compsn. is claimed.

Also claimed are (1) a pure yeast-derived EGF-like compsn. (B) having an equivalency of at least 943000ng of mouse-derived EGF activity/mg compsn.; (2) a process for the prodn. of (A) comprising extg. yeast with an alcohol and sepg. to obtain fraction (i), then reacting fraction (i) in an acidic medium with methanol, ethanol or acetone to obtain yeast EGF (fraction (ii)), which has an equivalency of at least 1000ng mouse-derived EGF activity/mg purified compsn.; and (3) a process for the prodn. of pure (2) comprising extg. yeast with an alcohol and sepg. to give fraction (i). This is purified by chromatography to obtain fraction (ii), which has an equivalency of at least 943000ng mouse-derived EGF activity/mg purified compsn.

USE/ADVANTAGE - EGF is used in medicinal compsns. to promote **wound** or burn healing, e.g. bed sores, decubitus **ulcers**, diabetic **ulcers** and other non-healing skin **ulcers**; as a skin protectant and in skin wrinkle control, e.g. photo-ageing, acne, psoriasis, dermatoses, insect bites and inflammation; in soft tissue and bone repair in orthopaedic and periodontal surgery; in control of post surgical adhesions in gastrointestinal, neurological and cardiac surgery; in ophthalmology as an aid to corneal transplant surgery and cataract removal; and to treat actinic keratoses. EGF administered orally is esp. used to promote healing of gastric and duodenal **ulcers** and to treat inflammatory bowel syndrome. Topical prods. to treat the above conditions are also provided. @

0/12vi

L141 ANSWER 81 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1990-253855 [33] WPIDS
CROSS REFERENCE: 1986-155752 [24]
DOC. NO. CPI: C1990-109926
TITLE: Stimulating hair growth with platelet derived factors - by applying platelet derived compsn. topically to tissue contg. hair follicles.
DERWENT CLASS: B04 D21
INVENTOR(S): KNIGHTON, D R; KNIGHTON, D R
PATENT ASSIGNEE(S): (CURA-N) CURATECH INC; (CURA-N) CURATIVE TECHNOLOGIES INC; (MINU) UNIV MINNESOTA; (MINU) MINNESOTA UNIVERSITY
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9007931	A	19900726	(199033)*		
RW: AT BE CH DE DK ES FR GB IT LU NL SE					
W: AU CA JP					
US 4957742	A	19900918	(199040)		
AU 9049647	A	19900813	(199044)		
EP 453498	A	19911030	(199144)		
R: AT BE CH DE ES FR GB IT LI LU NL SE					
JP 04504569	W	19920813	(199239)		4
US 5178883	A	19930112	(199305)		4
EP 453498	A4	19920415	(199521)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

US 4957742	A		US 1989-295406	19890110
EP 453498	A		EP 1990-902494	19900108
JP 04504569	W		JP 1990-502825	19900108
			WO 1990-US139	19900108
US 5178883	A	CIP of	US 1984-676471	19841129
		Cont of	US 1985-786206	19851018
		CIP of	US 1987-39776	19870415
		Cont of	US 1989-295406	19890115
			US 1990-525891	19900518
EP 453498	A4		EP 1990-902494	

FILING DETAILS:

PATENT NO	KIND		PATENT NO
JP 04504569	W	Based on	WO 9007931
US 5178883	A	Cont of	US 4957742

PRIORITY APPLN. INFO: US 1989-295406 19890110; US 1984-676471 19841129; US 1985-786206 19851010

AB WO 9007931 A UPAB: 19950425
Hair growth is promoted by topical application of a compsn. contg. (1) platelet-derived **growth factor** (A) and/or platelet-derived **angiogenesis** factor (B), or (2) materials (C) released from platelets. (A), (B) and (C) are mammalian, esp. human, products, derived from the subject being treated, or some other subject.
USE/ADVANTAGE - (A), (B) and (C) are useful for treating **wounds**, where they initiate/accelerate healing by increasing vascularisation, stimulating fibroblast mitosis and migration, and improving. collagen synthesis by fibroblasts. They are now found to stimulate hair growth. @(13pp Dwg.No.0/0)
0/0

L141 ANSWER 82 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1989-116296 [16] WPIDS
CROSS REFERENCE: 1995-358013 [46]; 1997-235537 [20]
DOC. NO. CPI: C1989-051344
TITLE: Aq. formulations contg. polypeptide **growth factor** - for topical or incisional **wound** healing esp. ophthalmic **wounds** also contain polymers of specific viscosities.
DERWENT CLASS: A96 B04 B07
INVENTOR(S): BEZWADA, R S; COHEN, J M; FINKENAUR, A L; KRONENTHAL, R L; SANDOVAL, E A; SHALABY, S W
PATENT ASSIGNEE(S): (ETHI) ETHICON INC
COUNTRY COUNT: 17
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 312208	A	19890419	(198916)*	EN	15
R: AT BE CH DE ES FR GB IT LI LU NL SE					
AU 8822235	A	19890323	(198920)		
PT 88541	A	19890731	(198935)		
JP 02000112	A	19900105	(199007)		
ZA 8806947	A	19900530	(199025)		
US 5427778	A	19950627	(199531)		10

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

EP 312208	A		EP 1988-308574	19880916
JP 02000112	A		JP 1988-232102	19880916
ZA 8806947	A		ZA 1988-6947	19880916
US 5427778	A	CIP of	US 1987-98816	19870918
		Cont of	US 1988-233483	19880819
		Cont of	US 1991-703584	19910520
			US 1992-974013	19921110

PRIORITY APPLN. INFO: US 1988-233483 19880819; US 1987-98816 19870918; US 1991-703584 19910520; US 1992-974013 19921110

AB EP 312208 A UPAB: 19980223

The novel formulations comprise (1) a gel for topical and incisional **wound** healing comprising (a) polypeptide **growth factor** (PGF) having human mitogenic or **angiogenic** activity; and (b) a water soluble or swellable polymer (WSP) providing viscosity of 1000-12000 000 cps at room temp., (2) a gel for healing **wounds** in the anterior chamber of the eye comprising (a) and a WSP providing viscosity of 10,000-100,000 cps at room temp.; and (3) (a) and a PGF providing a viscosity of 1-5,000 cps at room temp..

Pref. the PGF is epidermal, transforming-alpha, transforming-beta **basic fibroblast**, acidic fibroblast, insulin like platelet derived, **growth factor** or biologically active fragments or a deriv. or their mixts.. Esp. the PGF is epidermal **growth factor** (EGF) and is used in amt. of 0.01-1,000 mg/ml. Pref. in formulations (1) and (3) the polymer is (a) a vinyl polymer esp. poly(meth)acrylic acid, polyvinyl pyrrolidone or polyvinyl alcohol; (b) a polyoxyethylene-polyoxypropylene (PE/PP) copolymer; (c) a polysaccharide esp. a cellulose deriv. a glycosaminoglycan (in partic. hyaluronic acid, chondroitin, chonoroitin-4-sulphate, chondroitin-6-sulphate, dermatan sulphate, keratan sulphate, heparan sulphate or heporin) agor alginic acid, dextran, starch or chitosan; (d) a protein esp. collagen, gelatin or fibronectin; (e) a poly(ethylene oxide); or (f) acrylamide esp. polyacrylamide or polymethacrylamide.

USE/ADVANTAGE - The gel formulations (esp. th ose with viscosity) can be applied to gauze to form a **wound** healing bandage which stimulates cell growth and increases the rate of healing. The gels have a high water content keeping the **wound** moist, absorb **wound** exudate, have easy applicn. ano removal i .

Dwg.0/3

L141 ANSWER 83 OF 83 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1986-155752 [24] WPIDS
CROSS REFERENCE: 1990-253855 [33]
DOC. NO. CPI: C1986-066605
TITLE: **Wound** healing agent from blood - prepd. by isolating platelet-rich plasma and activating platelets.
DERWENT CLASS: B04
INVENTOR(S): KNIGHTON, R D; KNIGHTON, D R
PATENT ASSIGNEE(S): (MINU) UNIV MINNESOTA; (CURA-N) CURATECH INC; (CURA-N) CURATIVE TECHNOLOGIES INC
COUNTRY COUNT: 23
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8603122	A	19860605	(198624)*	EN	15
RW: AT BE CH DE FR GB IT LI LU NL SE					
W: AT AU BR CH DE DK FI GB HU JP KP LU NL NO SE SU					
AU 8550949	A	19860618	(198635)		
SE 8603228	A	19860725	(198643)		
NL 8520384	A	19861001	(198644)		

EP 202298	A	19861126 (198648)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE				
NO 8602964	A	19861027 (198650)		
DE 3590594	T	19870129 (198705)		
FI 8603087	A	19860728 (198719)		
DK 8603573	A	19860728 (198723)		
JP 62501628	W	19870702 (198732)		
HU 42329	T	19870728 (198733)		
CA 1261259	A	19890926 (198945)		
CH 673774	A	19900412 (199020)		
EP 383363	A	19900822 (199034)		
R: AT BE CH DE FR GB IT LI LU NL SE				
GB 2248777	A	19920422 (199217)		13
EP 202298	B1	19920715 (199229)	EN	6
R: AT BE CH DE FR GB IT LI LU NL SE				
DE 3586355	G	19920820 (199235)		
US 5165938	A	19921124 (199250)		5
IL 77096	A	19930131 (199311)		
GB 2248777	B	19930630 (199326)		
JP 07020873	B2	19950308 (199514)		4

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 8603122	A		WO 1985-US2205	19851108
NL 8520384	A		NL 1985-20384	19851108
EP 202298	A		EP 1985-905980	19851108
DE 3590594	T		DE 1985-3590594	19851108
JP 62501628	W		JP 1985-505204	19851108
EP 383363	A		EP 1985-106079	19851108
GB 2248777	A		GB 1986-17658	
EP 202298	B1		EP 1985-905980	19851108
			WO 1985-US2205	19851108
DE 3586355	G		DE 1985-3586355	19851108
			EP 1985-905980	19851108
			WO 1985-US2205	19851108
US 5165938	A	CIP of	US 1984-676471	19841129
		Cont of	US 1985-786206	19851010
		Cont of	US 1987-39776	19870415
			US 1990-526542	19900518
IL 77096	A		IL 1985-77096	19851119
GB 2248777	B		WO 1985-US2205	19851108
			GB 1986-17658	19851108
JP 07020873	B2		JP 1985-505204	19851108
			WO 1985-US2205	19851108

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 202298	B1	Based on	WO 8603122
DE 3586355	G	Based on	EP 202298
		Based on	WO 8603122
GB 2248777	B	Based on	WO 8603122
JP 07020873	B2	Based on	JP 62501628
		Based on	WO 8603122

PRIORITY APPLN. INFO: US 1984-676471 19841129; US 1985-786206 19851010

AB WO 8603122 A UPAB: 19950425
A process for producing physiologically active **wound** healing substances comprises (a) mixing blood with a citrate phosphate dextrose

soln. (**CPD**), (**b**) isolating platelet-rich plasma (PRP) from the blood, (c) activating the platelets and (d) combining the activated PRP with a microcrystalline collagen carrier. Pref. the platelets are activated with 1-10 units of thrombin per ml of 14P.

USE/ADVANTAGE - Throkbin activated platelets have the capacity to stimulate **angiogenesis**, increase collagen synthesis and cell division and growth. The prod. contains **angiogenic** and **growth factors** which may be used to speed the healing process of **wounds** by proliferating and directing the growth of capillary endothelium, doubling the rate of collagen synthesis and by producing leukocyte chemotaxis.

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